Dissertation on

A COMPARATIVE STUDY TO FIND THE OPTIMAL TIME TO INJECT SMALL DOSE FENTANYL TO OBTUND THE HAEMODYNAMIC RESPONSES TO LARYNGOSCOPY AND INTUBATION IN ENT PATIENTS

Dissertation Submitted in partial fulfillment of
the requirements for the degree of
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BRANCH X – ANAESTHESIOLOGY

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY
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CERTIFICATE

This is to certify that the Dissertation "**A COMPARATIVE STUDY TO FIND THE OPTIMAL TIME TO INJECT SMALL DOSE FENTANYL TO OBTUND HAEMODYNAMIC RESPONSES TO LARYNGOSCOPY AND INTUBATION IN ENT SURGERIES**" presented herein by **Dr.S.RAMESH KUMAR** is an original work done in the Department of Anaesthesiology, Madras Medical College and Government General Hospital, Chennai for the award of Degree of M.D. (Branch X) Anesthesiology under my guidance and supervision during the academic period of 2003-2006.

Place:
Date:

Prof.Dr.Kalavathy Ponniraivan, B.Sc**,** MD.,
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CERTIFICATE

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Place:
Date:

Prof.Dr.G.Sivarajan, MD., DA.,
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I will be failing in my duty if I do not express my heart felt gratitude to **Mr. G. Venkatesan**, M.Sc., the Statistician, Department of Community Paediatrics, Stanley Medical College, Chennai for his patient guidance and expert advice in the statistical analysis of the study data.

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INTRODUCTION

Hypertension and tachycardia occurring during laryngoscopy and endotracheal intubation in a light plane of anaesthesia has been reported since 1950 [24]. This increase in blood pressure and heart rate occurs most commonly from reflex sympathetic discharge in response to laryngotracheal stimulation, which in turn causes increased plasma norepinephrine concentration [16].The response following laryngoscopy and intubation peaks at 1.2 minutes and returns to baseline within 5 to 10 minutes.Though these sympathoadrenal responses are probably of little consequence in healthy individuals, it is hazardous to those with hypertension, coronary artery heart disease, intracranial pathology and hyperactive airways. In such cases, these responses need to be suppressed.

Tachycardia, hypertension and dysrhythmias all occur during laryngoscopy and intubation [29]. The consequent increase in Rate Pressure Product may result in a myocardial oxygen demand which exceeds the myocardial oxygen supply resulting in myocardial ischaemia. This response is sympathetically mediated. Prof King et al [24] documented myocardial ischaemic changes due to reflex sympathoadrenal response immediately following laryngoscopy and intubation with a mean increase in systemic pressure of 40 mm Hg even in normotensive patients.

An increase in heart rate is more likely to produce signs of myocardial ischaemia on the ECG than hypertension. Indeed, in anaesthetized patients, the incidence of myocardial ischaemia on the ECG increases in patients who experience a heart rate greater than 110 beats per minute (Ischaemic Threshold). A frequent recommendation is to maintain the heart rate and blood pressure within 20% of the normal awake value for that patient.

Many attempts have been made to attenuate the pressor response to laryngoscopy and intubation. They are:

1. Intubating in a deep plane of anaesthesia [35]
2. Use of topical anaesthesia [23,50]
3. Use of ganglionic blockers [44]
4. Use of intravenous local anaesthetics [50]
5. Use of arterial dilators – hydrallazine, SNP [49]
6. Use of venodilators – NTG [15]
7. Use of magnesium sulphate
8. Use of betablockers – Esmolol [12]
9. Ca channel blockers [36]
10. Use of opioids – Fentanyl, Morphine, Pethidine [1,2,3]

All the methods detailed above have their own advantages and disadvantages. High dose opioids have been used to attenuate circulatory responses to laryngoscopy and intubation more commonly and is supported by many studies. But high dose opioids have shortcomings like:

1) Producing undue sedation thereby becoming unsuitable for short procedures.
2) troublesome respiratory depression thereby delaying recovery; and may even require postoperative ventilatory support.
3) adverse effects like severe nausea and vomiting occurs more frequently with high doses.

To overcome these disadvantages, small dose opioids, especially Fentanyl is increasingly being used to effectively attenuate the stress response during anaesthetic induction. However, there have been only a few studies to evaluate the optimal time for injection of small dose Fentanyl to effectively obtund the secondary circulatory responses to laryngoscopy and endotracheal intubation.

Hence this study was designed to evaluate the optimal time for injecting small dose Fentanyl preoperatively, to effectively attenuate the

circulatory responses accompanying laryngoscopy and intubation during anaesthetic induction.

After getting approval from the hospital ethical committee, I carried out this study in the Department of Anaesthesiology, Madras Medical College and Government General Hospital, Chennai, during the period from November 2005 to February 2006.

AIM OF STUDY

To evaluate the optimal time for injecting small dose Fentanyl (2 μg / kg body wt) preoperatively to attenuate the circulatory responses to laryngoscopy and endotracheal intubation during anaesthetic induction.

ANATOMY – NERVE SUPPLY OF LARYNX

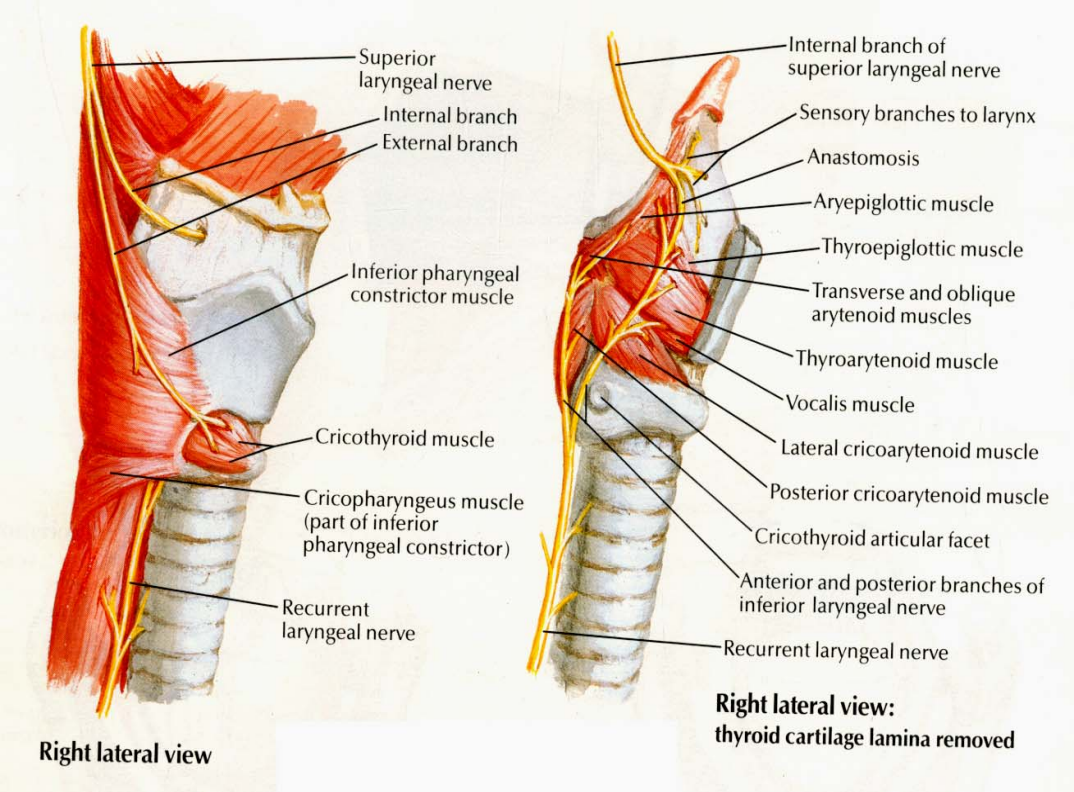
Nerve supply to the larynx is from the Superior laryngeal nerve and the Recurrent laryngeal nerve, both of which are branches of the vagus nerve.

The Superior laryngeal nerve arises from the middle of the inferior ganglion of the vagus, runs downwards and forwards on the superior constrictor muscle deep to internal carotid artery and reaches the middle constrictor muscle, where it divides into external laryngeal nerve and internal laryngeal nerve. External laryngeal nerve is thin, accompanies the superior thyroid artery, pierces the deep constrictor and ends by supplying the cricothyroid muscle.

Right recurrent laryngeal nerve arises from the vagus in front of the right subclavian artery, winds backwards below the artery to reach the tracheo-oesophageal groove. It is related to the inferior thyroid artery in its upper part. The nerve then passes deep to lower border of inferior constrictor muscle, and enters the larynx behind the cricothyroid joint. It supplies all the

intrinsic muscles of the larynx except the cricothyroid and carries sensory fibres to the larynx below the level of vocal cords.

The left recurrent laryngeal nerve arises from the vagus in the thorax. It curves around the aortic arch and soon gains entry into the tracheo-oesophageal groove. Thereafter its course is similar to that of the right recurrent laryngeal nerve.



PHYSIOLOGIC AND PATHOLOGIC RESPONSES TO DIRECT LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION

Intubation of the trachea alters respiratory and cardiovascular physiology by both reflex response and by the physical presence of an endotracheal tube. Although the reflex responses are generally of short duration and of little consequence in the majority of patients, they may produce profound disturbances in patients with underlying abnormalities such as hypertension, coronary artery heart disease, reactive airways and intracranial pathology.

The cardiovascular responses to laryngoscopy and intubation are bradycardia, tachycardia and hypertension; and they are mediated by both the sympathetic and parasympathetic nervous systems. Bradycardia is often seen in infants and small children during laryngoscopy and intubation. Although only rarely seen in adults, this reflex is mediated by an increase in vagal tone at the sinoatrial node and is virtually a monosynaptic response to a noxious stimulus in the airway.

The more common response to endotracheal intubation is hypertension and tachycardia mediated by sympathetic efferents via the cardioaccelerator nerves and sympathetic chain ganglia. The polysynaptic nature of pathways from the IX and X nerve afferents to the sympathetic nervous system via the brainstem and spinal cord results in a diffuse autonomic response which includes widespread release of norepinephrine from adrenergic nerve terminals and adrenal medulla.

Some of the hypertensive response to endotracheal intubation also results from activation of the Renin-Angiotensin system, with release of renin from the renal juxtaglomerular apparatus and endorgan innervated by beta adrenergic nerve terminals. The effects of endotracheal intubation on the pulmonary vasculature are probably less well understood than the responses elicited in the systemic circulation. They are often coupled with changes in airway reactivity associated with intubation. These are:

1) glottic closure reflex, i.e. laryngospasm due to brisk motor response
2) reduction in dead space
3) increase in airway resistance
4) bronchospasm as a reflex response to intubation
5) removal of the glottic barrier and may lower lung volume

6) cough efficiency is reduced

METHODS TO ATTENUATE CIRCULATORY RESPONSES DURING LARYNGOSCOPY AND ENDOTRACHEAL INTUBATION

The balance of myocardial oxygen supply and demand must be preserved to minimize the risk of perioperative ischaemia and infarction. Factors affecting myocardial oxygen supply are:

1) Heart rate

Supply depends upon diastolic time. Hence, lower the heart rate, more the diastolic time and more the oxygen supply to myocardium.

2) Coronary perfusion pressure

Depends on aortic diastolic pressure and ventricular end diastolic pressure and it increases with a high aortic diastolic pressure and low ventricular end diastolic pressure.

3) Arterial oxygen content

Depends on arterial oxygen tension and hemoglobin concentration.

4) Coronary vessel diameter

Supply is directly proportional to diameter of coronary vessel. Hence when the vessel is stenosed, the supply is reduced.

Factors affecting myocardial oxygen demand are

1) Basal requirement
2) Heart rate
3) Wall tension – Preload and afterload
4) Contractility

A number of methods were used to attenuate cardiovascular response due to laryngoscopy and endotracheal intubation. They are:

1) Deepening the plane of General Anaesthesia

The dose of volatile inhalational agents required to block the responses to endotracheal intubation is termed as MAC – ei. This deep level of anaesthesia achieved by inhalational agents results in profound cardiovascular depression prior to endotracheal intubation.The various agents that are used to obtund the intubation responses are Halothane, Isoflurane and Sevoflurane.

2) Lidocaine

The various modes by which lidocaine is used to attenuate the responses to direct laryngoscopy and endotracheal intubation are:

i) Lidocaine gargles for oropharyngeal anaesthesia

ii) Aerosol for intratracheal anaesthesia

iii) Topical spray over the cords

iv) Regional nerve blocks

   a) Superior Laryngeal Nerve

   b) Glossopharyngeal nerve

v) Intravenous bolus for systemic anaesthesia

Topical anaesthesia of the upper airway has proven to be less effective than systemic administration of lidocaine.

Mechanism of action of lidocaine

1) By increasing the depth of anaesthesia
2) Potentiation of the effects of N2O anaesthesia and reduction of MAC of Halothane by 10 to 28 %
3) Direct cardiac depression
4) Peripheral vasodilatation
5) Antiarrythmic properties
6) Suppression of cough reflex

3) Vasodilators

1. Hydralazine
2. Sodium Nitroprusside
3. Nitroglycerine

4) Narcotics

1. Fentanyl
2. Alfentanyl
3. Sufentanil
4. Remifentanyl
5. Morphine
6. Pethidine

Of these, Fentanyl is the most commonly used narcotic agent to attenuate the responses to intubation.

Mechanism of action

a) suppresses the nociceptive stimulation caused by intubation.
b) centrally mediated decrease in sympathetic tone (Lambie et al 1974).
c) Activation of vagal tone.

5) Adrenergic Blockers

α receptor blockers: Phentolamine

β receptor blockers: Esmolol, Metaprolol, Propranol

α and β receptor blockers: Labetalol

Of these, Esmolol is the most commonly used agent because of its ultrashort duration of action.It reduces resting heart rate, systolic blood pressure, rate pressure product, ejection fraction and cardiac index; but it maintains the coronary perfusion pressure.

6) Calcium Channel Blockers

Nifedipine, Nicardipine, Diltiazem, Verapamil

Of these, Diltiazem is the most commonly used drug though Nicardipine has superior actions.

7) α2 agonist

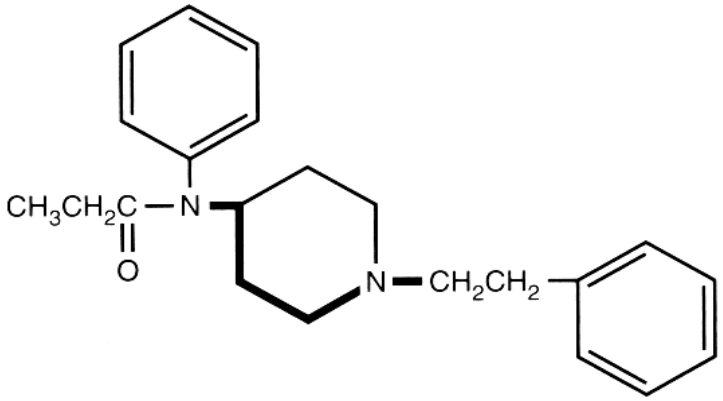
Clonidine – it acts by suppressing the increase in sympathetic activity produced by laryngoscopy and intubation.

8) Midazolam: Sedative and anxiolytic

9) Magnesium Sulphate: Sedative and anxiolytic

PHARMACOLOGY OF FENTANYL

Fentanyl, the first of the present generation of potent aniline-piperidine opioids, as introduced into clinical practice in the mid-1960s. It was shown to be 80 – 100 times as potent as morphine, with a high therapeutic index, shorter duration of action, more specific, and with fewer adverse effects than morphine. Fentanyl is a synthetic opioid which acts at the μ receptors as an agonist.



PHARMACODYNAMICS

I) **ACUTE EFFECTS**

1) CENTRAL NERVOUS SYSTEM EFFECTS

a) Analgesia

b) Sedation

c) Euphoria

d) Respiratory depression

e) Cough suppressant

f) Miosis

g) Nausea and vomiting

h) Skeletal muscle rigidity

2) CARDIOVASCULAR EFFECTS

a) Bradycardia – central vagal stimulation in high doses

b) No effect on cardiac contractility

c) Hypotension , especially in large doses due to bradycardia, venodilatation and suppression of central sympathetic outflow

3) RESPIRATORY SYSTEM EFFECTS

Dose dependent respiratory depression through direct action

a) Apnoic threshold increased

b) Hypoxic drive decreased

c) Chest wall rigidity causes decrease in lung compliance

d) Delayed respiratory depression

4) GASTROINTESTINAL TRACT EFFECTS

a) Delays gastric emptying

b) Causes biliary colic

5) ENDOCRINE SYSTEM EFFECTS

a) Attenuation of stress response

6) MISCELLANEOUS

b) Histamine release

c) Smooth muscle spasm

II) **CHRONIC EFFECTS**

a) Tolerance

b) Physical dependence

MECHANISM OF ACTIONS

1) ANALGESIA AND MOOD EFFECTS

a) The processing of pain information is inhibited by a direct spinal effect on the dorsal horn of spinal cord.

b) Rostral transmission of pain signals is decreased by activation of descending inhibitory pathways in the brainstem.

c) Emotional response to pain is altered by opioid actions on the limbic cortex.

d) Act at receptors located peripherally on the sensory neurons.

2) RESPIRATORY DEPRESSION

Direct effect on respiratory centers in the medulla.

3) ANTITUSSIVE

Direct effect on cough centers in the medulla.

4) MIOSIS

Stimulation of the Edinger – Westphal nucleus of the oculomotor nerve.

5) NAUSEA AND VOMITING

Stimulation of Chemoreceptor Trigger Zone complex interaction of dopaminergic, cholinergic or serotonergic mechanisms.

6) MUSCLE RIGIDITY

By acting at the receptors in the striatum, it increases the rate of striatal dopamine biosynthesis and inhibits the release of the inhibitory neurotransmitter Gamma Amino Butyric Acid (GABA).

7) CARDIOVASCULAR SYSTEM

a) Bradycardia – stimulation of central vagal nuclei
b) Peripheral vasodilatation – depression of vasomotor centre in the medulla
c) Decreased central sympathetic tone – raising the arrhythmogenic threshold
d) Hypotension – especially in patients with elevated sympathetic tone due to hypovolumia and cardiac failure.

8) TOLERANCE

a) Acute tolerance or tachyphylaxis
b) Chronic tolerance

c) Cross tolerance to other opioid agonists

Tolerance develops most rapidly to the depressant effects of opioids.

PHARMACOKINETICS

Fentanyl is a potent synthetic opioid, which is extremely fat soluble and has a rapid onset and a relatively short duration of action. After intravenous administration, it is rapidly distributed to the brain, heart and other highly perfused areas. It readily crosses the blood brain barrier and the placental barrier. Peak effect occurs in 3 – 5 minutes. Within a short time, the drug distributes extensively throughout the body so that the plasma level falls precipitously. This large concentration gradient thus produced favours the redistribution of Fentanyl away from the central nervous system and thus terminates its effect. When redistribution is almost completed, the elimination phase begins so that the plasma levels fall much more slowly.

METABOLISM

Fentanyl is biotransformed in the liver to inactive metabolites, primarily to Norfentanyl and several hydroxylation products. Only 6 to 8 % of the drug is excreted unchanged in the urine. The hepatic clearance of the drug is high (12 to 13 μg / kg body wt / minute). When given orally, the first pass metabolism is nearly 60%. The large volume of distribution however means that the drug remains extravascular and hence available for biotransformation.

The long elimination half life of Fentanyl (3 – 4 hrs) is a function of the slow rate at which the drug reenters the central compartment. Fentanyl concentration in plasma correlates well with cerebrospinal fluid concentration and pharmacodynamic effects. Fentanyl pharmacokinetics therefore predicts some of the most important pharmacodynamic properties. When low doses (1 – 3 μg / kg body wt) of Fentanyl are administered, redistribution terminates the effect and hence the drug appears short acting. In large doses (> 20 μg / kg body wt), redistribution is not sufficient to terminate the effect and so it depends on the elimination process which is slow and hence the drug appears long acting. Repeated intravenous boluses are likely to cause cumulative effects. High hepatic extraction ratio (0.6%) means that the clearance is limited by hepatic blood flow.

ROUTES OF ADMINISTRATION

Due to high first pass metabolism by the liver, oral route is inefficient. The most reliable route is intravenous. The drug is also well absorbed transdermally, intranasally and by the oral mucosa.

ADVERSE EFFECTS

a) Respiratory depression
b) Apnoea
c) Muscular rigidity

d) Bradycardia

e) Hypotension

f) Dizziness

g) Blurred vision

h) Nausea and vomiting

i) Laryngospasm

j) Diaphoresis

DOSAGE AND ADMINISTRATION

Dosages should be individualized. Some of the factors that should be considered while determining the dose are age, bodyweight, physical status, underlying pathological condition, use of other drugs, type of anaesthesia to be used and the surgical procedures involved. One problem with Fentanyl was the wide inter-individual variability, as typified in the paper of Reilly and colleagues [2], who described a wide range of variability in disposition within seven different sets of parameters. The different dosage schedules commonly followed are:

1) PREMEDICATION

50 – 100 µg may be administered intramuscularly 30 to 60 minutes before surgery.

2) ADJUNCT TO GENERAL ANAESTHESIA

In the 1990s, the optimal strategy for dosing with Fentanyl is probably that of "Balanced Anaesthesia", where Fentanyl is supplemented by Isoflurane or another volatile agent. To provide analgesia, plasma drug concentrations need to be around 1-2 ng / ml; this can best be achieved using a loading dose of 2-8 μg / kg body wt and an infusion thereafter of 0.5 – 3.0 μg / kg / hr. However, there is a problem with infusing Fentanyl for intraoperative anaesthesia – this highly lipid-soluble drug is significantly liable to accumulate in lipophilic peripheral tissues, with a resulting marked increase in the "context sensitive halftime ".

a) LOW DOSE (2 μg / kg body wt)

In small doses, it is most useful for minor but painful surgical procedures. In addition to analgesia during surgery, it may also provide some pain relief in the immediate postoperative period.

b) MODERATE DOSE (2 – 20 μg / kg body wt)

In this dose, in addition to adequate analgesia, one would expect to see abolition of the stress response. However respiratory depression will be such that artificial ventilation during anaesthesia is necessary and careful observation of ventilation postoperatively is also essential.

c) HIGH DOSE (25 – 50 μg / kg body wt)

This dose is usually used for open heart surgeries and certain complicated neurosurgical and orthopaedic surgeries where surgery is more prolonged and in the opinion of the anaesthesiologist, the stress response to surgery would be detrimental to the well being of the patient. This high dose along with N2O and O2 have been shown to attenuate the stress response as defined by increasing levels of circulating Growth Hormone, Catecholamines, ADH and Prolactin.

3) AS A GENERAL ANAESTHETIC

When attenuation of the responses to surgical stress is especially important, doses of 50-100 μg/kg may be administered with O2 and muscle relaxant. This technique has been reported to provide anaesthesia without the use of additional anaesthetic agents. In certain cases, doses up to 150 μg / kg body wt may be necessary to produce this anaesthetic effect.

4) ADJUNCT TO REGIONAL ANAESTHESIA

50 – 100 μg may be administered intramuscularly or slowly intravenously over one to two minutes, when additional analgesia is required.

5) POSTOPERATIVELY

50 -100 μg may be administered intramuscularly for the control of pain, tachypnoea and emergence delirium. The dose may be repeated in one to two hours as needed.

TREATMENT OF OVERDOSAGE

a) Hypoventilation / Apnoea : Oxygen administration ,maintain patent airway with an oropharyngeal airway or by an endotracheal tube; assist or control the ventilation

b) Truncal rigidity: Intravenous neuromuscular blocking agents may be required to assistor control ventilation if it is affecting the respiration.

c) Hypotension : Appropriate parenteral fluids

d) Respiratory depression : Use opioid antagonists like Naloxone, Naltrexone, Nalorphine, Levallorphan.

REVIEW OF LITERATURE

REID & BRACE (1940) postulated that reflex circulatory responses to laryngeal instrumentation were mediated through the vagus nerve and they named it as "Vaso Vagal Reflex".

KING et al (1951) [24] used deep ether anaesthesia to abolish the reflex circulatory response to tracheal intubation.

WYCOFF.C.C. (1960) [53] in his study stated that topical anaesthesia of the pharynx along with superior laryngeal nerve blocks reduced the increase in mean arterial pressure after intubation.

STEIMHANS & GASKIN (1963) [48] found that intravenous lignocaine suppressed the cough reflex. It is very easy to predict that if the cough is suppressed, the rise in blood pressure, pulse rate and intracranial pressure noticed on laryngeal instrumentation would be blunted by this technique.

FORBES and DALLY (1970) [16] observed that laryngoscopy and endotracheal intubation is immediately associated with an average increase in mean arterial pressure of 25 mmHg in all 22 normotensive patients. These responses were interpreted as due to reflex adrenal stimulation.

MASSON and ECKANKOFF (1971) proved that the hypertensive response in patients can be significantly decreased by simple lignocaine spray.

PRYS ROBERTS et al (1971) [40] found that the increase in heart rate and blood pressure are much more exaggerated in hypertensive patients.

DENLINGER.J.K. and ELLISON.N.E. (1974) [10] have used intratracheal lignocaine spray which causes a 50% reduction in the hypertensive response.

VICTORIA FARIA BLANC and NORMAND.A.G. (1974) in their article of "complications of tracheal intubation" have classified the neurogenic or reflexly mediated complication into three different categories.

a) Laryngo Vagal Reflexes – which gives rise to spasm of the glottis, bronchospasm, apnoea, bradycardia, cardiac dysrhythmias and arterial hypotension. The mere presence of the tracheal tube seem to be the most common cause of bronchospasm in anaesthetized asthmatic patients.

b) Laryngo Sympathetic Refexes – which include tachycardia, tachyarrhythmia and acute arterial hypertension as frequent

complications. The hypertensive, hyperdynamic state during laryngoscopy may be related in some cases to an increased nor-adrenaline fraction of the total catecholamines.

c) Laryngo Spinal Reflexes – which include coughing, vomiting and bucking.

TAMMISTO.T & AROMAA.U (1977) [52] has shown in his study that tolerance to the endotracheal tube is more rationally achieved by small doses of narcotic analgesics (e.g. fentanyl 0.5 to 1 μg / kg) than by increasing the dosage of thiopentone.

RYHANEN P, SAARELA E, SAUKKONEN J, HOLLMEN A (1977) [42] suggested that administration of a small prophylactic dose of Practolol is useful in preventing the excessive cardiovascular response due to laryngoscopy and tracheal intubation.

CURREN and CROWLEY M et al (1980) [8] in their study showed that Droperidol 150 μg/kg given intravenously before anaesthesia attenuated the pressor response to laryngoscopy and intubation.

McCAMMON RL et al (1981) [28] showed in their study that intravenous Propranolol does not ensure protection against increases in HR and MAP associated with laryngoscopy and intubation of the trachea.

FASSOULAKI A, KANIARIS P (1983) [15] proved in their study that intranasal administration of nitroglycerine attenuates the pressor response to laryngoscopy and intubation of the trachea.

TAM.S. et al (1985) [51] found attenuation of circulatory responses to laryngoscopy and endotracheal intubation using intravenous lignocaine; a determination of the optimal time as 3 minutes before intubation.

BATRA Y.K, INDU.B, PURI.G.D (1988) [4] observed that oral clonidine attenuated the pulse rate and blood pressure response to laryngoscopy and tracheal intubation.

DONALD.R.MILLER and RAYMOND.J.MARTINEAN (1989) [12] used bolus dose of Esmolol for treating hypertension, tachycardia and myocardial ischaemia intraoperatively.

NISHIKAWA T, NAMIKI A (1989) [36] proved in their study that intravenous Verapamil attenuates the pressor response to laryngoscopy and tracheal intubation.

HATANO Y, IMAI R, KOMATSU K, MORI K (1989) [21] showed in their study that intravenous administration of isosorbide dinitrate attenuates the pressor response to laryngoscopy and tracheal intubation.

T.NISHINO, K. HIRAGA and K. SUGIMORI (1990) [38] proved that lignocaine had a dose dependent effect on the extubation reflex, cough reflex in patients anaesthetized with enflurane, and that 1.5 mg/ kg of intravenous lignocaine can suppress the cough reflex and other related reflexes during intubation, extubation, bronchoscopy and laryngoscopy when duration of these procedures is relatively brief.

C.D.MILLER and S.J.WARREN (1990) [34] observed that intravenous lignocaine given within three minutes had no significant effect on cardiovascular effects of laryngoscopy and intubation.

MIKAWA K, MAEKAWA N, GOTO R, KAETSU H, HASEGAWA M, YAKU H, OBARA H (1991) [29] showed that a bolus dose of Pindolol 4 μg

/ kg body wt is a simple, practical and effective method for attenuating cardiovascular responses to laryngoscopy and intubation.

MIKAWA K, MAEKAWA N, GOTO R, YAKU H, OBARA H, KASUNOKI M (1991) [31] concluded in their study that 2 or 3 mg / kg body wt of Diazoxide given 2.5 minutes before laryngoscopy attenuates pressor response to intubation.

MIKAWA K, MAEKAWA N, GOTO R, KAETSU H, , YAKU H, OBARA H (1991) [30] showed in their study that ATP 0.05 mg / kg or 0.1 mg / kg bolus injection is a simple, practical and effective method for attenuating the hypertensive response to laryngoscopy and tracheal intubation.

MIKAWA K, MAEKAWA N, GOTO R, KAETSU H, HASEGAWA M, YAKU H, OBARA H (1992) [32] concluded in their study that intravenous Mexiletine 3 mg / kg body wt is a simple method for attenuating pressor response to intubation.

SAITOH N and MIKAWA K et al (1992) [44] in their study found that intravenous Trimetaphan 0.05 – 0.1 mg / kg body wt given 1.75 min before the start of laryngoscopy may be used as a supplement during induction, to

attenuate the hypertensive response associated with laryngoscopy and tracheal intubation.

MIKAWA K and MAEKAWA N et al (1992) [33] in their study has concluded that oral Nilvadipine 2mg or 4mg before induction is a simple and practical method for attenuating pressor response to laryngoscopy and intubation.

CHUNG KS and SINATRA RS et al (1992) [7] in their study showed that Labetalol 0.4 mg/kg blunted the HR response to laryngoscopy and intubation during rapid sequence induction in healthy patients but had a minimal effect on Blood pressure.

LICKER M, FARINELLI C, KLOPFENSTEIN CE (1995) [26]concluded in their study that thoracic epidural blockade combined with general anaesthesia was associated with preserved baroreflex function, and it afforded haemodynamic protection during laryngoscopy and intubation in the elderly.

DURRANI M, BARWISE JA, JOHNSON RF, KAMBAM JR, JANICKI PK (2000) [13] showed that intravenous chloroprocaine attenuates hemodynamic changes associated with direct laryngoscopy and tracheal intubation.

KITAMURA T, YAMADA Y, CHINZEI M, DU HL, HANAOKA K (2001) [25] showed in their study that using the new intubation device Styletscope helps in the attenuation of hemodynamic responses to tracheal intubation.

YOO KY, JEONG ST, HA IH, LEE J (2003) [54] showed that Nitrous oxide attenuates pressor but augments norepinephrine response to laryngoscopy and endotracheal intubation.

GOYAGI T, TANAKA M, NISHIKAWA T (2005) [20] concluded in their study that continuous administration of Landiolol before tracheal intubation results in the attenuation of cardiovascular response for tracheal intubation.

DAHLGREN.N & MESSETER.K (1981) [9] in their study showed that fentanyl in the dose of 5 μg / kg body wt when given before induction with thiopentone and succinylcholine caused a significant attenuation of the blood pressure and pulse response to laryngoscopy and intubation.

DONAL.E.MARTIN (1982) [11] has also proved the efficacy of a low dose Fentanyl along with an induction dose of Thiopentone. But in these

series, it was found that the incidence and occurance of tachycardia was not prevented.

. KAUTTO VM (1982) [22] studied attenuation of circulatory response to laryngoscopy and intubation with Fentanyl 6µg / kg body wt had concluded that this dose completely abolished these responses.

MARTIN.D.E & ROSENBERG.H et al (1982) has showed that doses of fentanyl that are low enough to cause little postoperative respiratory depression significantly blunt postintubation hypertension when used as an adjunct to thiopental.

BLACK.T.E & KAY B et al (1984) [5] in their study showed that Alfentanyl in dose of 15 µg/kg reduces the cardiovascular responses to laryngoscopy and intubation and the effect appears to have a shorter duration than that of fentanyl 5µg/kg body wt.

CHUNG F & EVANS D (1985) [6] proved in their study that fentanyl 3 µg/kg when used as an adjunct to barbiturate induction, effectively lowered the thiopentone requirement and attenuated the pressor response to laryngoscopy and intubation.

KAY B, T.E.I.HAECY and P.M.BOLDER (1985) compared Fentanyl and Nalbuphine in blocking the circulatory responses to laryngoscopy and tracheal intubation and found that nalbuphine attenuated mean pressure response to these manoeuvers but had no effect on the accompanying tachycardia whereas Fentanyl 5μg/kg prevents these responses however at the cost of significant decrease in both blood pressure and heart rate and increased incidence of respiratory depression.

FUSCIARDI.J & GODET.G et al (1986) [17] in their study on patients with stable angina undergoing operations of short duration has shown that fentanyl 3μg / kg plus a continuous intravenous nitroglycerin infusion, 0.9 μg / kg / min in addition to thiopentone and pancuronium anaesthetic induction significantly decreases the incidence of myocardial ischemia associated with induction of anaesthesia and tracheal intubation.

LINDGREN L & SAARNIVAARA.L (1987) [27] in their study has proved that fentanyl in doses of 1 2 or 3 μg/kg body wt provided adequate protection against cardiac arrhythmias during induction of anaesthesia and also showed that it did not prevent the prolongation of QT interval after succinylcholine.

ACALOVSCHI.I & SZILAGY.E et al (1989) [1] has proved that fentanyl in the dose of 5 μg/kg when used as preinduction agent to etomidate ensured the blockage of the pressor response to intubation, with hemodynamic stability during anaesthesia induction.

P.EBERT, JANES.D PEARSON.MD (1989) [14] compared the effects of placebo, Fentanyl and Esmolol and found the HR responses to laryngoscopy and intubation was more effectively blocked by Fentanyl while Esmolol better retained perfusion pressure.

SPLINTER WM, CERVENKO F (1989) [47] has concluded in their study that both Lignocaine and Fentanyl are recommended adjuncts to induction of anaesthesia with Thiopentone in geriatric patients.

SIMS C.H & SPLINTER W.M (1990) [45] in their study has proved that fentanyl blunts the hemodynamic response of children to laryngoscopy.

GAUBATZ CL & WEHNER R.J (1991) [18] concluded in their study that Esmolol in doses of excess of 1 mg/ kg appear to be necessary for effective control of heart rate. However when used with fentanyl, esmolol provides effective protection against the adrenergic response to laryngoscopy and intubation.

SMITH J.E & KING.M.J et al (1992) [46] in their study has proved the effectiveness of Fentanyl 6μg/mg in attenuating the cardiovascular effects of fibreoptic intubation under general anaesthesia.

CHUNG.K.S, SINATRA.R, HARLEUY J.D, PAIGE D (1992) [7] compared Fentanyl, Esmolol and their combination for blunting the haemodynamic responses during rapid sequence induction and concluded that the combination of low dose Fentanyl and Esmolol provides an alternative to a higher dose of Fentanyl for blunting the hemodynamic responses to laryngoscopy and intubation.

NISHINA.K & MIKAWA.K et al (1995) [37] in their study has shown that fentanyl 2 μg/kg attenuated the increases in HR, SBP and DBP more effectively than fentanyl 1 μg/kg and concluded that a bolus dose of fentanyl 2 μg/kg given at the time of peritoneal closure was of value in attenuating the cardiovascular changes associated with tracheal extubation and emergence from anaesthesia, and that this treatment did not prolong the recovery.

ADACHI.Y, TAKAMATSU.I & HARADA.M et al (1998) [3] in their study compared the effects of fentanyl 4 μg/kg, Pentazocine 0.5 mg / kg and buprenorphine 5 μg/kg administered 5 minutes before thiopentone

induction and concluded that only fentanyl 4 μg/kg diminished the circulatory responses of systolic blood pressure on the stimuli of endotracheal intubation.

PANG.W.W & LEI CH et al (1999) [39] showed in their study that Tramadol 3 mg/kg when given right before Thiopentone induction did not display a better attenuation against the increase of haemodynamic profiles than did Fentanyl 3μg/kg following tracheal intubation.

ADACHI YU & SATAMOTO.M et al (2002) [2] in their study has concluded that Fentanyl attenuates the hemodynamic response to endotracheal intubation more than the response to laryngoscopy.

SAHIHOGLU.Z & DEMIROLUK.S (2002) [43] compared the effects of fentanyl 1μg/kg, Alfentanyl 10μg/kg and Remifentanyl 1μg/kg followed by an infusion of 0.5 pg/kg/min in ASA physical status I & II morbidly obese patients and concluded that all the three had similar effects in controlling the haemodynamic response to tracheal intubation.

MATERIALS AND METHODS

A study was conducted to examine the optimal time for injecting small dose Fentanyl during anaesthetic induction to attenuate circulatory responses to laryngoscopy and endotracheal intubation in patients posted for elective ENT surgeries. The study comprised 80 patients in the age group 20 to 50 years. Both male and female patients posted for ENT surgeries were included for the study. All the patients were informed of the study and prior written informed consent was obtained. The surgeon was also informed of the study.

Patients were assessed by a detailed physical examination supported by investigations like routine blood tests- Hb, blood sugar, blood urea, serum creatinine, serum electrolytes, Chest X ray PA view, Electrocardiogram, etc.

INCLUSION CRITERIA

1) Patients in ASA physical status I & II
2) Patients with modified Mallampatti scores I & II
3) Age 20 to 50 years

EXCLUSION CRITERIA

1) Patients in ASA physical status III & IV
2) Patients with modified Mallampatti scores III & IV
3) Patients with predicted difficult airway
4) Obese patients
5) Patients with Systemic Hypertension, Coronary Artery Heart Disease, H/O Cerebrovascular Accidents, Chronic Renal Failure, Valvular Heart Diseases, patients on antihypertensives or cardiac drugs
6) Patients posted for emergency surgeries
7) Patients with full stomach
8) If the intubation time has exceeded 15 seconds
9) Age < 20 and > 50 years

In this study, patients were randomly assigned into 4 groups:

Group I: 20 patients were given Inj Pentazocine (500 µg / kg body weight) 5minutes before intubation: which served as the control group.

Group II: 20 patients were given Inj Fentanyl (2 µg / kg body weight) 1 minute before intubation.

Group III: 20 patients were given Inj Fentanyl (2 μg / kg body weight) 5 minutes before intubation.

Group IV: 20 patients were given Inj Fentanyl (2 μg / kg body weight) 10 minutes before intubation.

ANAESTHESIA PROTOCOL

Preoperative visit was made to allay anxiety, and a good rapport was established with the patient.

PREMEDICATION

All patients were given Tab Diazepam 10 mg orally the night before surgery. Tab Ranitidine 150 mg was given at 7 am on the morning of surgery. All patients were given Inj Glycopyrrolate 5 μg / kg body wt intramuscularly 45 minutes before surgery.

MONITORING

Patients were shifted to the operating room and connected to a standard multimonitor – ECG, NIBP and pulse oximeter. NIBP was recorded every minute for the initial period up to 10 minutes after endotracheal

intubation.The average of the first two preoperative values recorded 3 minutes apart were noted down which represented the operating room baseline values.

INDUCTION AND INTUBATION

Patients were given Inj Fentanyl 2µg / kg body wt either 1 minute, 5 minutes or 10 minutes before laryngoscopy and endotracheal intubation according to the group to which they were assigned. Patients in the control group received Inj.Pentazocine 500µg / kg body weight 5 minutes before intubation. Patients were preoxygenated for 3 minutes. A priming dose of Vecuronium Bromide (0.01mg / kg body wt) was given; followed 4 minutes later by Inj Thiopentone Sodium (5mg / kg body wt). Inj Vecuronium (0.1 mg / kg body wt) was then given one minute after Thiopentone. Thereafter all the patients were manually ventilated with bag and mask with100% oxygen for 3 minutes. Laryngoscopy and intubation was then done and the time taken for the same was noted. Those that took more than 15 seconds were excluded from the study. After confirmation of the endotracheal tube position, anaesthesia was maintained for the next 3 minutes with 67% Nitrogen and 33% Oxygen. No surgical stimulation was permitted for 5 minutes after intubation. The baseline, preintubation, during intubation, 1 minute after

intubation and 3 minutes after intubation values of circulatory variables such as heart rate and systolic blood pressure were recorded.

Changes in each circulatory variable after tracheal intubation were based on the differences between baseline values and values obtained 1 minute after intubation. The baseline and 1 minute postintubation values of HR and SBP were compared. In addition these circulatory variables were compared among the groups.

Hypertension was defined as an increase in SBP more than 120% of the patient's baseline value. Hypotension was defined as SBP less than 70 % of the patient's baseline value. Tachycardia and bradycardia were defined as a heart rate greater than 120 bpm and less than 60 bpm respectively. A dysrhythmia was defined as any ventricular or supraventricular premature beat or any sustained rhythm that is other than sinus rhythm. Depression of spontaneous respiration before thiopentone was defined as a fall in SPO2 value to less than 92% with an oxygen mask. Chest rigidity was defined as an increase in the resistance to bag and mask ventilation. Delayed recovery was defined as the failure of the patient to wake up even 20 minutes after the termination of anaesthesia, thus preventing or delaying the extubation of the trachea. Postoperative respiratory depression was defined as a fall in

respiratory rate to less than 12 and a fall in SPO2 value to less than 92% in the post anaesthesia care unit.

The incidence of hypertension, hypotension, tachycardia, bradycardia, any dysrhythmias, depression of spontaneous respiration, delayed recovery and postoperative respiratory depression were recorded throughout the study period and in the immediate postoperative period and were compared among the groups.

All results were expressed as mean ± SD. The data were analysed using a repeated measures- analysis of variance (ANOVA) for within group comparisions. Differences among groups were analysed using a one-way ANOVA. A Tukeys test was used when a significant difference was indicated with the ANOVA procedure. Complication rates among patients were analysed using $\chi 2$ test. A P value of < 0.05 was considered statistically significant.

OBSERVATION AND RESULTS

Eighty patients under this study were categorized into four groups, 20 in each group. They comprised both sexes in the age group 20 to 50 years. The demographic profile is as follows:

AGE DISTRIBUTION

AGE DISTRIBUTION IN THE FOUR GROUPS

Table 1

Age(yrs)	Group I	Group II	Group III	Group IV	Total
21 – 30	5	8	6	5	24
31 – 40	7	8	5	6	26
41 – 50	8	4	9	9	30

AGE GROUP (yrs) Table 2

Group	N	Mean	Std. Deviation	F-test
Control	20	36.40	8.469	F=0.49 P=0.69
Group II	20	33.05	9.006	
Group III	20	35.05	9.186	
Group IV	20	34.88	8.609	

$\chi 2=4.04$ P=0.67 (P value of significance being < 0.05)

The age distribution between the four groups are equal – the difference is insignificant. (P=0.67).

SEX DISTRIBUTION

Table 3

Sex	Group I	Group II	Group III	Group IV	Total
Male	9	8	10	13	40
Female	11	12	10	7	40

$\chi 2=2.80$ P=0.42 (P value of significance being < 0.05)

The sex distribution between the four groups are equal as shown in the bar chart, the difference being insignificant (P = 0.42).

WEIGHT DISTRIBUTION (Kgs)

Table 4

GROUP	N	Mean(kgs)	Sd	F-test
Group I	20	52.85	3.774	F=0.34 P=0.79
Group II	20	52.95	3.576	
Group III	20	52.70	3.570	
Group IV	20	53.75	3.447	

P value of significance being < 0.05.

Weight distribution is also equal between these groups (P = 0.79)

The four groups that were included in the study were:

Group I: 20 patients were given Inj Pentazocine (500 µg / kg body weight) 5minutes before intubation (Control)

Group II: 20 patients were given Inj Fentanyl (2 µg / kg body weight) 1 minute before intubation.

Group III: 20 patients were given Inj Fentanyl (2 µg / kg body weight) 5 minutes before intubation.

Group IV: 20 patients were given Inj Fentanyl (2 µg / kg body weight) 10 minutes before intubation.

The heart rate and systolic blood pressure were the circulatory variables that were measured in this study. The operation room baseline value of these two variables was noted first. The preintubation, during intubation, 1 minute after intubation and 3 minutes after intubation values of these two variables were noted.

There were no significant differences among the groups in the baseline values of systolic blood pressure and heart rate. There were significant differences among the groups with respect to the preintubation, during intubation, 1 minute and 3 minutes after intubation values of SBP and HR. Changes in SBP and HR was greatest 1 minute after intubation. Hence

these values were therefore used for comparison with the baseline values to determine whether there were intergroup as well as within group differences.

SYSTOLIC BLOOD PRESSURE CHANGES IN THE FOUR GROUPS

Table 5

SBP (mm Hg)	CONTROL		GROUP II		GROUP III		GROUP IV	
	MEAN	SD	MEAN	SD	MEAN	SD	MEAN	SD
BASELINE	120.85	6.18	124.50	7.13	118.40	4.33	120.60	8.34
PRE INTUBATION	121.50	6.32	123.10	6.57	117.30	4.17	116.60	8.21
DURING INTUBATION	124.40	6.85	133.05	4.94	121.05	4.35	119.60	8.07
1 MIN AFTER INTUBATION	150.70	8.18	150.55	4.72	131.00	3.70	141.00	10.26
3 MINS AFTER INTUBATION	140.00	7.02	143.30	4.60	126.50	4.35	132.70	10.16

SYSTOLIC BLOOD PRESSURE CHANGES

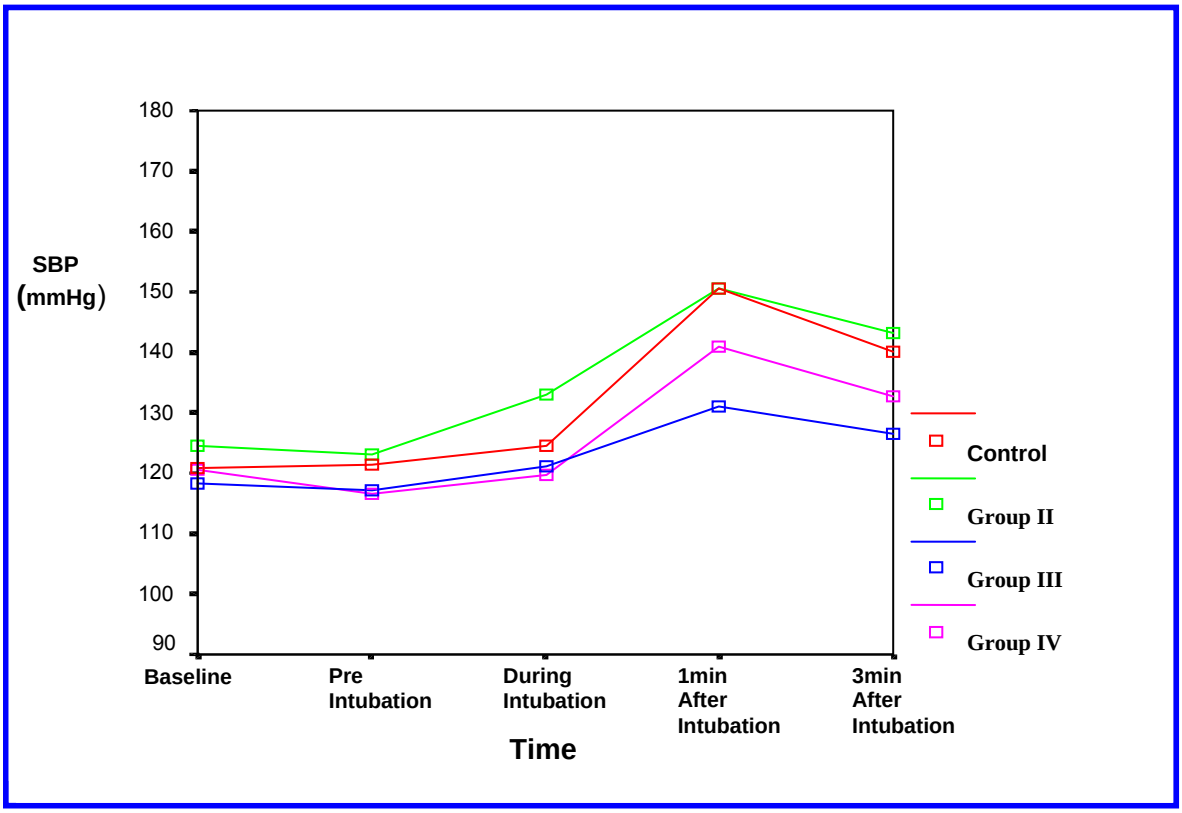


Table 5 shows the Mean SBP changes of all the four Groups recorded during the study. The graph depicts the Mean SBP values of all the four groups recorded in the study. The baseline values of all the four groups was found to be more or less similar, as shown in the graph which was found to have no statistical difference between the four groups.

The preintubation value of Mean SBP in Group I was 121.5 ± 6.32 mm Hg, which increased 124.40 ± 6.85 mm Hg during intubation. It further

increased to 150.70 ± 8.18 mm Hg 1 minute after intubation. This rise in mean SBP 1 minute after intubation when compared to the baseline value was statistically significant. It can be noted that the mean SBP did not return to near baseline value even 3 minutes after intubation. All the values remained above the other three groups.

The preintubation mean SBP in Group II was 123.10 ± 6.57 mm Hg which increased to 133.05 ± 4.94 mm Hg during intubation. The value further increased to 150.55 ± 4.72 mm Hg 1 minute after intubation. This increase in SBP from the baseline value was statistically significant. The mean SBP remained at 143.30 ± 4.60 mm Hg 3 minutes after intubation showing that the stress response was not significantly attenuated. All the values in Group II were just below the control group with the mean SBP 1 minute after intubation in both the groups more or less equal. The increase in mean SBP from baseline in both groups showed that there was no effective attenuation of pressor responses to intubation in both these groups.

In Group III, the preintubation mean SBP was 117.30 ± 4.17 mm Hg. This value increased to 121.05 ± 4.35 mm Hg during intubation. The value recorded 1 minute after intubation was 131.00 ± 3.70 mm Hg. This increase in mean SBP from baseline to 1 minute after intubation was not statistically significant. The value at 3 minutes after intubation was 126.50 ± 4.35 mm Hg. It can be seen from the graph above that the values in this group were below

the other three groups, proving that the pressor responses to laryngoscopy and intubation were better attenuated compared to the other three groups.

In Group IV, the preintubation mean SBP was 116.60 ± 3.21 mm Hg, increasing to 119.60 ± 8.60 mm Hg during intubation. I minute after intubation, the mean SBP increased to 141.00 ± 10.26 mm Hg. This increase in mean SBP from baseline was not statistically significant. The mean SBP 3 minutes after intubation was 132.70 ± 10.16 mm Hg. It can be seen from the graph that in group IV also there was attenuation of pressor responses to intubation next only to Group III but better than the other two groups.

It can be seen from the graph that the mean SBP after intubation returned to near the baseline values quicker in groups III and IV as shown by the values at 3 minutes after intubation, again proving that the pressor responses were better attenuated in these two groups when compared to the control group and group I.

The data obtained from all the four groups were analysed by the Repeated Measures of Variance (ANOVA) for within group comparisions. Differences among groups were analysed using a One Way ANOVA.(Table 6)

REPEATED MEASURES OF ANOVA

Table 6

SBP differences	F	Sig.
Within group	656.7	.001
Between group	16.666	.001

(P value of significance being < 0.05)

A Tukey's test was used when a significant difference was indicated with the ANOVA procedure. Table 7 shows the multiple comparisions among the four groups by the Tukey's test. There was no statistical difference between the control group and Group II (Fentanyl given I minute before intubation) [P > 0.05]. A statistically significant difference was observed between the control group and Group III (Fentanyl given 5 minutes before intubation) [P = 0.000]. There was also a statistically significant difference observed between the control group and Group IV (Fentanyl given 10 minutes before intubation) [P=0.026].

MULTIPLE COMPARISONS

Table 7

(I) group	(J) group	Mean Difference (I-J)	Sig.
Control	Group II	-3.41	.269
	Group III	**8.64(*)**	**.000**
	Group IV	**5.39(*)**	**.026**
Group II	Control	3.41	.269
	Group III	**12.05(*)**	**.000**
	Group IV	**8.80(*)**	**.000**
Group III	Control	**-8.64(*)**	**.000**
	Group II	**-12.05(*)**	**.000**
	Group IV	-3.25	.310
Group IV	Control	**-5.39(*)**	**.026**
	Group II	**-8.80(*)**	**.000**
	Group III	3.25	.310

***** The mean difference is significant at the 0.05 level**.**

The difference between Group III and Group IV was statistically insignificant, meaning that these two groups were more or less equal in their effort to attenuate the stress responses to intubation. But from the graph, since Group III has the least mean SBP values 1 minute after intubation, Group III showed the best attenuation of increase in SBP associated with intubation.

HEART RATE CHANGES IN THE FOUR GROUPS

Table 8

HR (PER MINUTE)	CONTROL		GROUP II		GROUP III		GROUP IV	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
BASELINE	78.60	5.28	77.30	6.30	77.00	6.82	77.60	6.67
PRE INTUBATION	83.30	3.76	69.90	4.13	74.20	5.62	67.45	4.29
DURING INTUBATION	102.05	8.36	98.60	11.41	81.80	4.05	84.00	6.99
1 MIN AFTER INTUBATION	121.20	7.88	118.60	6.65	97.55	9.73	112.30	10.94
3 MINS AFTER INTUBATION	111.85	9.26	108.60	6.87	94.10	4.88	91.65	10.50

HEART RATE CHANGES

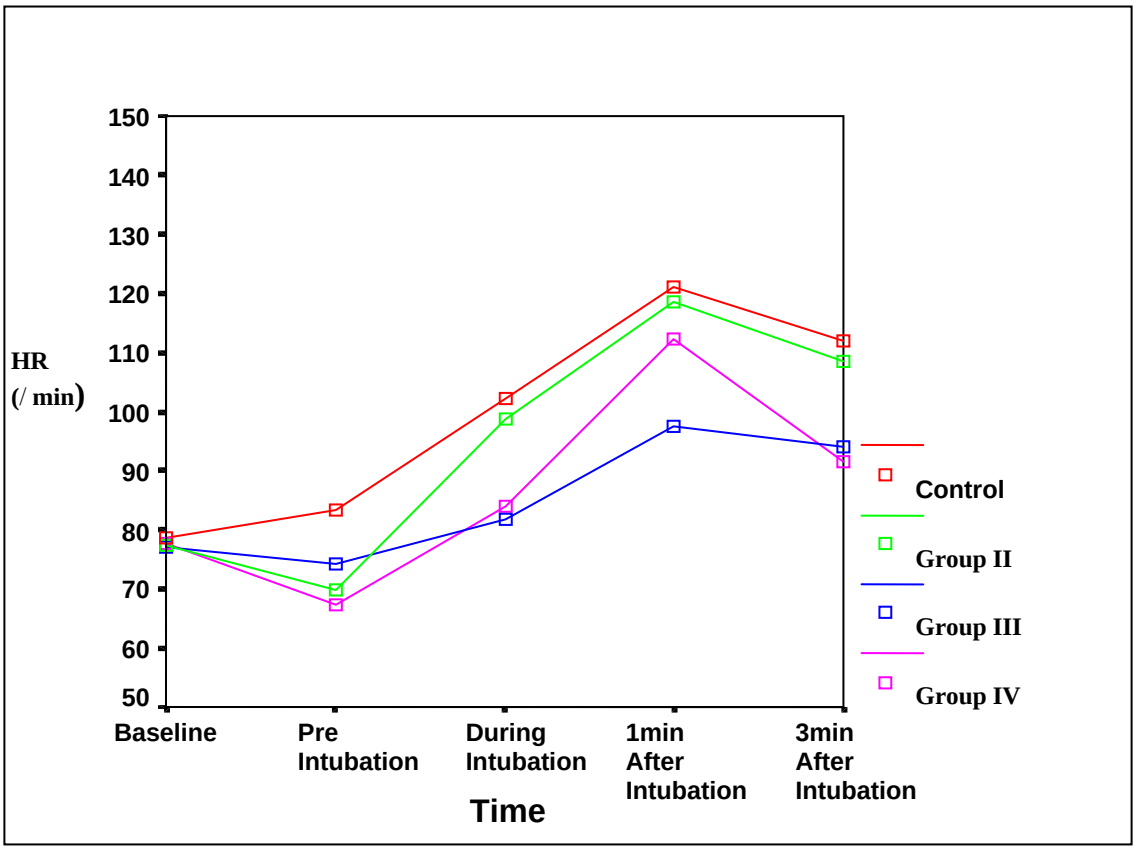


Table 8 shows the mean HR changes of all the four groups including the baseline value and that recorded during the study – preintubation, during intubation, one minute and three minutes after intubation. The graph below is a graphical representation of these values. From the graph, it can be noted that the baseline mean HR in all the four groups were more or less similar and there was no statistical difference between the groups with regard to the baseline value.

In Group I or the control group, the preintubation mean HR was 83.30 ± 3.76 per minute, which increased to 102.05 ± 8.36 per minute during intubation. The mean HR further increased to 121.20 ± 7.88 per minute. This increase in HR from baseline is statistically significant. The mean HR three minutes after intubation was 111.85 ± 9.26 per minute. There was no attenuation of stress response in the control group, and all the values in this group remained above the other three groups.

In Group II where fentanyl was given one minute before intubation, the preintubation mean HR was 69.90 ± 4.13 per minute. The mean HR increased to 98.60 ± 11.41 per minute during intubation. The mean HR at I minute after intubation was 118.60 ± 6.65 per minute and this increase from the baseline value was statistically significant. The mean HR remained at 108.60 ± 6.87 per minute three minutes after intubation.

In Group III, the preintubation value was 74.20 ± 5.62 per minute. The mean HR increased to 81.80 ± 4.05 per minute during intubation. This further increased to 97.55 ± 9.73 per minute one minute after intubation.The increase in mean HR from the baseline was statistically not significant. The mean HR came to 94.10 ± 4.88 per minute three minutes after intubation. From the graph it can be noted that the values remained significantly closer to

the baseline value, meaning that the stress response to intubation was better attenuated in this group.

The preintubation mean HR in Group IV was 67.45 ± 4.29 per minute which increased to 84.00 ± 6.99 per minute during intubation. This further increased to 112.30 ± 10.94 per minute one minute after intubation. This increase from baseline was statistically not significant. The mean HR three minutes after intubation was 91.65 ± 10.50 per minute. In this group also, the stress response was attenuated, but less than Group III and significantly better than the other two groups.

The mean HR returned to near the baseline value in Groups III & IV much earlier than the other two groups, meaning that better hemodynamic stability was attained in Groups III & IV.

The data of mean HR values from the four groups were analysed by the Repeated Measures of ANOVA for within group comparisions. Differences among groups were analysed using a one way ANOVA (Table 9).

REPEATED MEASURES OF ANOVA

Table 9

HR differences	F	Sig.
Within group	501.6	.001
Between group	43.6	.001

(P value of significance being < 0.05)

Both the HR differences within group (P = 0.001) and between group (P = 0.001) were found to be statistically significant.

A Tukey's test was used when a significant difference was indicated with the ANOVA procedure. Table 10 shows the multiple comparisions among all the four groups. A statistically significant difference was observed between the groups except between Group III & Group IV.

MULTIPLE COMPARISONS

Table 10

(I) group	(J) group	Mean Difference (I-J)	Sig.
Control	Group II	**4.80(*)**	**.008**
	Group III	**14.47(*)**	**.000**
	Group IV	**12.80(*)**	**.000**
Group II	Control	**-4.80(*)**	**.008**
	Group III	**9.67(*)**	**.000**
	Group IV	**8.00(*)**	**.000**
Group III	Control	**-14.47(*)**	**.000**
	Group II	**-9.67(*)**	**.000**
	Group IV	-1.67	.662
Group IV	Control	**-12.80(*)**	**.000**
	Group II	**-8.00(*)**	**.000**
	Group III	1.67	.662

* The mean difference is significant at the 0.05 level.

COMPLICATIONS

The complications noted during the study were hypertension, tachycardia, bradycardia, truncal rigidity, depression of spontaneous respiration, dysrhythmia, delayed recovery and post operative respiratory depression. (Table 11)

Table 11

COMPLICATIONS	GROUP I	GROUP II	GROUP III	GROUP IV	Sig
Tachycardia	10	8	1	6	$\chi 2$= 0.41 **P = 0.02**
Bradycardia	0	5	9	12	$\chi 2$ = 0.34 **P = 0.04**
Hypertension	12	5	2	5	$\chi 2$= 2.86 **P= 0.004**
Hypotension	0	0	0	0	NIL
Chest rigidity	0	0	1	1	$\chi 2$ = 2.05 P = 0.56
Dysrhythmia	2	1	2	0	$\chi 2$ = 2.35 P = 0.50
Depression of Spontaneous ventilation	0	0	1	5	$\chi 2$ = 1.32 **P = 0.03**
Delayed recovery	0	0	0	0	NIL
Post operative Respiratory depression	0	0	1	0	$\chi 2$ = 2.12 P = 0.42

(P value of significance being < 0.05)

The incidence of tachycardia was high in the control group and in Group II and lowest in Group III. This difference was statistically significant.

There was a high incidence of bradycardia in Group IV (12 patients), followed by Group III with 9 patients. There was no case of bradycardia in the control group. The hemodynamic stability was not affected in any of these patients and only 4 out of the 26 patients actually required Inj Atropine sulphate 0.6 mg IV to treat it. The difference was statistically significant.

Control group had the highest incidence of hypertension (12 patients), followed by Group II and Group IV with 5 patients each. Group III had the least incidence (2 patients). This difference was statistically significant. Hypotension was not noted in any of the patients in the four groups.

There were two cases of chest rigidity, one each in groups III and IV. Both these patients were effectively managed with bag and mask ventilation.

Dysrhythmias occurred in 5 cases. All of these were ventricular ectopic beats, which disappeared spontaneously without any intervention. There was no haemodynamic instability in any of these five patients.

Depression of spontaneous ventilation as noted by a fall in the SPO2 value to less than 92 % in room air occurred in 5 cases in group IV and in 1 patient in group III. These patients were then given assisted ventilation with bag and mask in 100 % oxygen. This difference was statistically significant.

There was no case of delayed recovery in any of the groups. There was 1 patient in group III who had post operative respiratory depression, as noted by the fall in SPO2 value to less than 92% in room air, 20 minutes after extubation. He was effectively managed with 100% O2 in Venturi mask at the Post operative care unit. However, there was no statistically significant difference.

DISCUSSION

Laryngoscopy and tracheal intubation are usually accompanied by increases in arterial blood pressure and heart rate [29]. This response is undesirable, especially in patients with cardiovascular and intracranial disease. Increase in heart rate and blood pressure occurs most commonly from reflex sympathetic discharge in response to laryngotracheal stimulation, which in turn leads to increased norepinephrine levels.

Induction of anaesthesia is a critical phase in the anaesthetic procedure. Sympathetic response, coughing and straining during laryngoscopy and endotracheal intubation should be avoided. The transient nature of hypertension and tachycardia, that usually lasts about 10 minutes during laryngoscopy and intubation, might be the reason for the fewer incidences of complications in the normotensive patient. However in patients with compromised heart or with neurological disease, such transient nature of hypertension may itself precipitate heart failure and intraventricular haemorrhage.

Many methods have been suggested to attenuate the circulatory responses to laryngoscopy and endotracheal intubation. They are the use of

inhaled anaesthetics [35], sympathetic blockers [44], vasodilators [49], local anaesthetics [50], narcotics [3] and a combination of these drugs.

Many studies have reported a beneficial effect of fentanyl as an adjunct to barbiturate induction. Dahlgren and Messeter [9] have shown that 5 µg / kg of fentanyl given before intubation effectively blunts the cardiovascular stress responses to intubation in neurosurgical patients. Using 8 µg / kg fentanyl preloading, Martin et al. [11] demonstrated that fentanyl abolishes both the heartrate and blood pressure increases related to tracheal intubation and prevents an increase of pulmonary capillary wedge pressure during the induction of anaesthesia with thiopentone.

. Nishina.K & Mikawa.K et al (1995) [37] in their study has shown that fentanyl 2 µg/kg attenuated the increases in HR, SBP and DBP more effectively than fentanyl 1 µg/kg and concluded that a bolus dose of fentanyl 2 µg/kg given at the time of peritoneal closure was of value in attenuating the cardiovascular changes associated with tracheal extubation and emergence from anaesthesia, and that this treatment did not prolong the recovery.

Adachi.Y, Takamatsu.I & Harada.M et al (1998) [2] in their study compared the effects of fentanyl 4 µg/kg, Pentazocine 0.5 mg / kg and buprenorphine 5 µg/kg administered 5 minutes before thiopentone induction

and concluded that only fentanyl 4 µg/kg diminished the circulatory responses of systolic blood pressure to the stimulation of endotracheal intubation. Unlike sympathetic blockers, vasodilators and local anaesthetics, fentanyl can produce potentially disturbing side effects, such as skeletal muscle rigidity and postanaesthetic respiratory depression. Chung and Evans [6] investigated the effects of 3µg/kg of fentanyl in geriatric patients and found that, fentanyl attenuated increases in heart rate and arterial pressure during the first minute after intubation, compared with controls.

Since fentanyl in large doses that were initially used to attenuate circulatory responses to intubation produce many side effects, small dose Fentanyl is increasingly being used to effectively attenuate the stress response during anaesthetic induction. However there has been no evaluation of the optimal time of injection of small dose Fentanyl to effectively obtund the secondary circulatory responses to laryngoscopy and endotracheal intubation. Hence this study was designed to evaluate the optimal time for injecting small dose Fentanyl to effectively attenuate the circulatory responses accompanying laryngoscopy and intubation during anaesthetic induction. For this study I used Inj. Fentanyl 2 µg / kg body weight before induction based on the study made by Nishina.K & Mikawa.K et al (1995) [37] who showed that this dose effectively blunted the increase in SBP, DBP, MAP and HR that accompanies

laryngoscopy and intubation. Young et al (1998) [55] had done a similar study using Fentanyl 2µg/kg to obtund the intubation response.

I compared the effectiveness of fentanyl given 1 minute, 5 minutes and 10 minutes before intubation in obtunding the stress response to intubation, as shown by the increase in SBP and HR that follows laryngoscopy and intubation. I compared the effectiveness between the three groups and also with a control group which did not receive fentanyl. Since the maximum stress is at one minute after intubation, I took it as the cut off point to compare the effectiveness in attenuating the increase in SBP and HR from the baseline.

SYSTOLIC BLOOD PRESSURE CHANGES

In the study done by Young et al [55], the control group did not receive fentanyl. Since we routinely use Inj. Pentazocine as an analgesic during induction of anaesthesia for most of the cases in our hospital, I used Pentazocine in the control group. The stress response to laryngoscopy and intubation was not attenuated in the control group as shown by the statistically significant increase in the mean SBP value (150.7±8.18 mmHg) recorded at 1 minute after intubation from the baseline. This finding was in concordance

with the study done by Young et al [55] as well as with the study done by Adachi et al [3].

In group II where fentanyl was given 1 minute before intubation, the increase in mean SBP from baseline to 1 minute after intubation (150.55±4.72 mmHg) was also statistically significant, indicating that the stress response to laryngoscopy and intubation was not adequately obtunded. This finding was also in concordance to the study by Young et al (151±14 mmHg).

When fentanyl was given 5 minutes before intubation as in Group III, the increase in mean SBP from baseline to 1 minute after intubation was the least among the four groups (131±3.7 mmHg). This increase was not statistically significant proving that the pressor response to laryngoscopy and intubation was adequately obtunded in this group. This finding was also in accordance with the study by Young et al. This finding also correlated well with the study of Chung & Evans [6], as well as with Splinter & Cervenko [47].

In Group IV, the increase in mean SBP recorded at 1 minute after intubation from the baseline value (141±10.26 mmHg) was statistically not significant. This showed that the pressor response to intubation was

adequately attenuated in this group. This finding however was not in concordance with the study by Young et al (151±26).

From the above findings, both Group III and Group IV showed adequate attenuation of stress response to laryngoscopy and intubation. Multiple comparisions among the four groups by the Tukeys test (Table 7) showed that there was no statistical difference between groups I and II, as well as between Groups III and IV.

Since the increase in mean SBP at 1 min after intubation was the least in Group III, it can be concluded that the pressor response to laryngoscopy and intubation is best attenuated when Fentanyl is given 5 minutes before intubation, which is consistent with the peak analgesic effect of Fentanyl.

HEART RATE CHANGES

In the control group, the increase in mean heart rate recorded 1 minute after intubation from the baseline was statistically significant (121.2±7.88). This increase was the highest recorded among the four groups showing that there was no attenuation of stress response to laryngoscopy and

intubation. This finding was in concordance with the study done by Young et al and by Adachi et al.

In Group II, there was a statistically significant increase in the mean heart rate from the baseline to that recorded at 1 minute after intubation (118.6±6.65). This increase was the second highest recorded among the groups. This showed that there was no attenuation of stress response in Group II as well. This finding was in concordance with the finding by Young et al.

Patient in Group III who received Fentanyl 5 minutes before intubation showed adequate attenuation of stress response as shown by the increase in heart rate from baseline which was not statistically significant (97.55±9.73). Also, it can be recalled from the graph that the value recorded is the least among the groups. This finding was also in concordance with the study made by Young et al.

In group IV, the increase in heart rate from the baseline to 1 minute after intubation was not statistically significant (112.3±10.94). This shows that there was adequate attenuation of stress response to laryngoscopy and intubation in patients receiving fentanyl 10 minutes before intubation. This

finding was not in concordance with Young et al who showed that there was no adequate attenuation in this group.

In table 10, the multiple comparisions among groups showed that there was no statistically significant difference between groups III and IV. In this study, both Group III and Group IV showed adequate attenuation of stress response to laryngoscopy and intubation. Since the increase in mean heart rate was the least in Group III, it can be concluded that the attenuation of stress response to laryngoscopy and intubation is best achieved by giving low dose fentanyl 5 minutes before intubation, which is consistent with its peak analgesic effect. This finding was in concordance with the study by Young et al.

COMPLICATIONS

Hypertension was defined as an increase in SBP more than 120% of the patient's baseline value. Hypotension was defined as SBP less than 70 % of the patient's baseline value. Tachycardia and bradycardia were defined as a heart rate greater than 120 bpm and less than 60 bpm respectively. A dysrhythmia was defined as any ventricular or supraventricular premature beat or any sustained rhythm that is other than sinus rhythm. Depression of spontaneous respiration before thiopentone was defined as a fall in SPO2

value to less than 92% with an oxygen mask. Chest rigidity was defined as an increase in the resistance to bag and mask ventilation. Delayed recovery was defined as the failure of the patient to wakeup even 20 to 30 minutes after the termination of anaesthesia, thus preventing or delaying the extubation of the trachea. Postoperative respiratory depression was defined as a fall in respiratory rate to less than 12 and a fall in SPO2 value to less than 92% in the post anaesthesia care unit. These complications were recorded throughout the study period and compared among the groups.

Hypertension occurred mostly in Groups I and II (12 and 5 respectively). This difference was statistically significant. This showed that the attenuation to pressor response to laryngoscopy and intubation was not adequate in these two groups. This was in concordance to the study done by Young et al. Only 7 out of the 40 patients in groups III and IV had hypertension, proving that the stress response was better obtunded in these two groups.

Tachycardia also followed the same pattern showing higher incidence in groups I and II (10 and 8 respectively). This was also statistically significant. Group III (1patient) had the least incidence followed by Group IV (6 patients), again proving that there was better attenuation of stress response in these groups. This was also in accordance to Young et al.

Peroperative bradycardia occurred commonly in groups III and IV (9 and 12 respectively). There was no case of bradycardia in the control group. This also was in concordance to the study by Young et al. Bradycardia is a well recognized side effect of fentanyl. In this study, though 26 patients had bradycardia, none of them resulted in any haemodynamic instability. Only 4 required Inj Atropine sulphate 0.6 mg IV stat to treat it.

Truncal rigidity or chest rigidity was seen in 2 patients (1 each in groups III and IV). This is also another recognized troublesome side effect of fentanyl. But in both these cases, there was no interference with ventilation, and it was effectively managed with bag mask assisted ventilation. This was statistically not significant. Young et al in his study had no case of chest rigidity in his patients.

Dysrhythmias were noted in only 5 patients, 2 in Group I, 1 in Group II and 2 in Group III. All of these were ventricular premature beats. None of these cases had hemodynamic instability. All of these disappeared spontaneously. There was no statistically significant difference. Young et al in his study noted dysrhythmias mainly in the control group. Lindgren and Saarnivaara (1987) [27] in their study proved that fentanyl in doses of 1, 2 or 3µg/kg body wt provided adequate protection against cardiac arrhythmias

during induction of anaesthesia. But in my study, I noted dysrhythmias in 3 of the fentanyl treated patients.

Depression of spontaneous ventilation occurred mostly in Group IV (5 patients). This is also a well recognized side effect of fentanyl. Since the time interval between administering fentanyl and the actual anaesthetic induction was high (around 7-8 minutes) in Group IV, this might be the reason for the higher incidence of this complication in this group. In my study, none of the patients in all the groups were left unattended after giving fentanyl remembering this potential complication. Once the SPO2 fell to 92% in room air, 100% O2 was administered through bag and mask.

Post operative respiratory depression occurred in only 1 patient in Group III. This is also a recognized side effect of Fentanyl. He was efficiently managed at Post anaesthesia care unit. He eventually recovered in one hour. This was also not statistically significant.

SUMMARY

This study evaluated the optimal time for administering Fentanyl in the dose of 2 μg / kg body wt, in attenuating the stress response to laryngoscopy and intubation during anaesthetic induction.

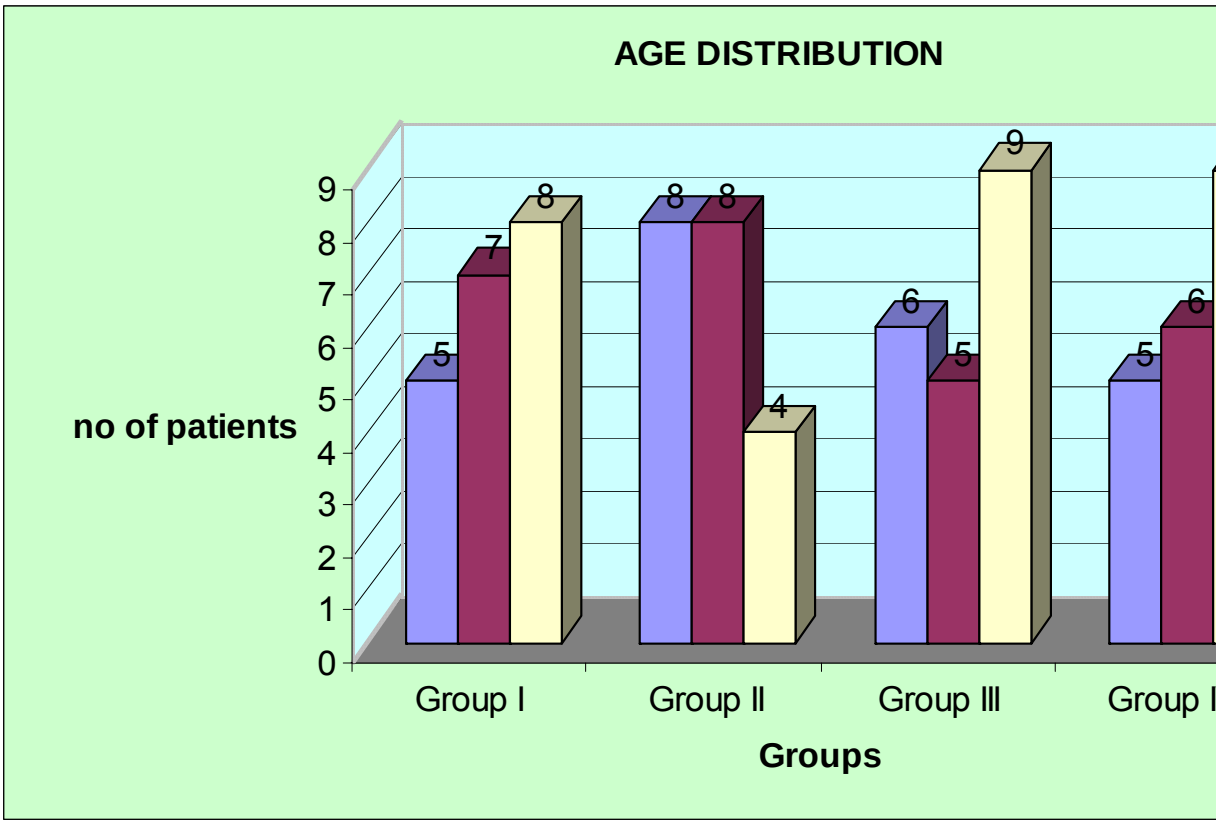
From the data, it was found that both the Systolic blood pressure and heart rate changes that follow laryngoscopy and intubation were well obtundated, when fentanyl was given 5 minutes before intubation. Also, it was observed that the complications due to fentanyl were minimum in this group.

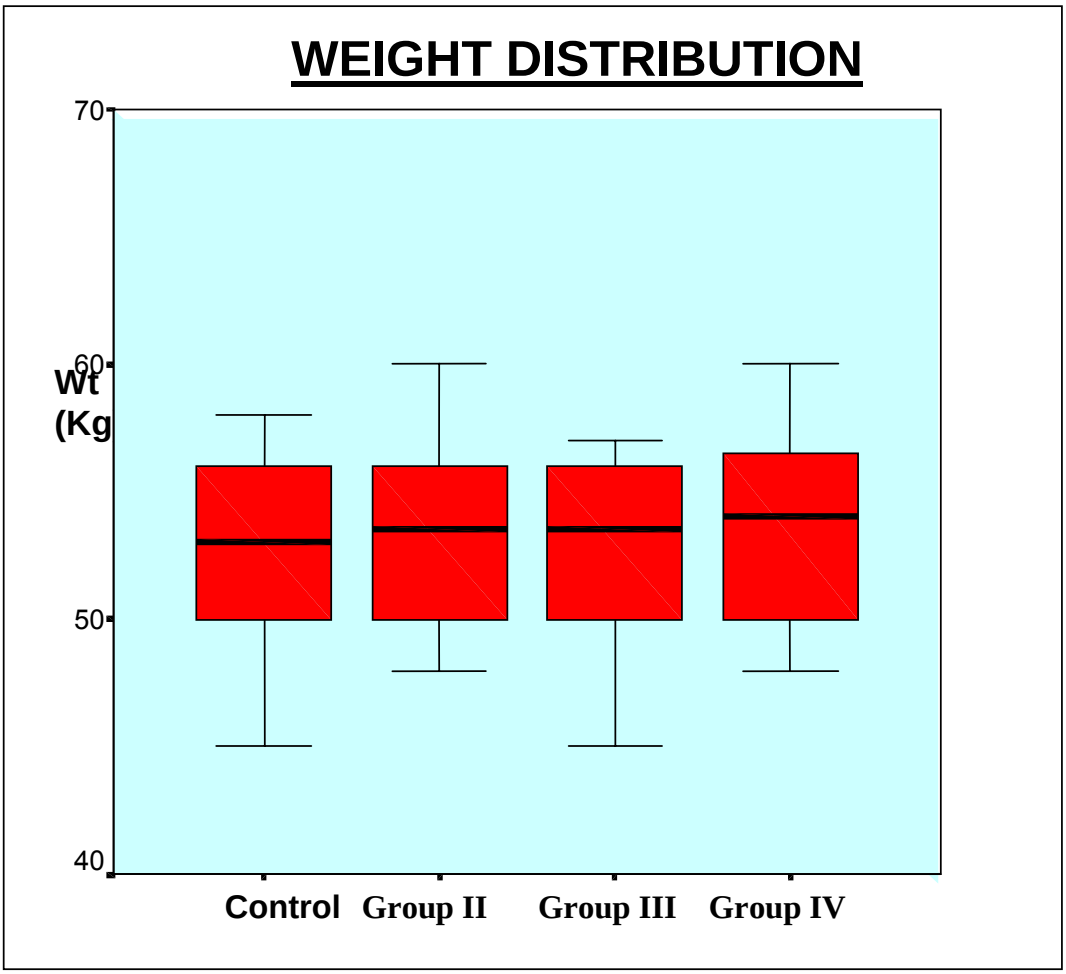
The study thus shows that, Inj Fentanyl 2 μg / kg body wt when given 5 minutes before intubation showed the maximum attenuation of the hemodynamic responses that accompany laryngoscopy and endotracheal intubation during anaesthetic induction.

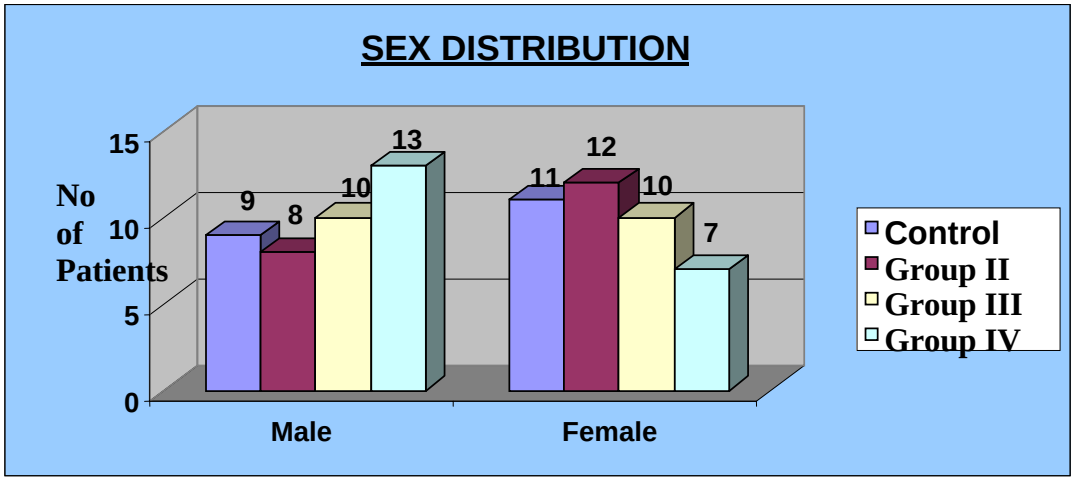
CONCLUSION

Fentanyl in the dose of 2µg/kg body weight when given 5 minutes before intubation adequately attenuates the circulatory response to laryngoscopy and endotracheal intubation without producing major complications.

AGE DISTRIBUTION IN THE FOUR GROUPS




WEIGHT DISTRIBUTION
70
60
50
40
Wt (Kg
Control
Group II
Group III
Group IV


SEX DISTRIBUTION
15
10
5
0
No of Patients
9
8
10
13
11
12
10
7
Male
Female
Control
Group II
Group III
Group IV

CONTROL GROUP –HEART RATE

S. No	Name	Age (yrs)	Sex	Weight (kgs)	SYSTOLIC BLOOD PRESSURE (mm Hg)				
					Baseline	Pre Intubation	During Intubation	1 min after intubation	3 min after intubation
1	Kumar	48	M	55	174	76	102	124	12
2	Rekha	36	F	56	176	81	104	109	10
3	Karthik	25	M	52	182	82	112	128	12
4	Perumal	44	M	58	180	84	102	108	10
5	Kasthuri	32	F	45	184	82	112	132	12
6	Ramanan	41	M	51	186	84	96	116	11
7	Nagamma	37	F	50	182	82	106	146	13
8	Suresh	22	M	55	80	86	92	118	10
9	Ramani	46	F	56	82	88	103	128	11

CHANGES (beats per minute)

10	Rajendran	38	M	55	78	84	89	118	11
11	Kavitha	27	F	48	76	82	104	116	10
12	Balaji	44	M	50	72	80	102	115	9
13	Suganthi	28	F	56	70	82	98	124	10
14	Ponnaiyan	48	M	58	68	75	112	118	10
15	Akila	33	F	54	78	82	96	122	10
16	Madhavan	45	M	58	74	80	98	114	10
17	Mariammal	35	F	52	78	84	102	126	12
18	Rukmani	41	F	50	80	86	100	116	10
19	Fathima	37	F	50	82	86	94	124	11
20	Jennifer	21	F	48	84	88	93	128	12

CONTROL GROUP – SYSTOLIC BLOOD PRESSURE CHANGES (mm Hg)

8	Suresh	22	M	55	132	132	132	158	1
9	Ramani	46	F	56	124	124	124	155	1
10	Rajendran	38	M	55	124	126	128	160	1
11	Kavitha	27	F	48	122	130	134	146	1
12	Balaji	44	M	60	120	118	120	150	1
13	Suganthi	28	F	50	116	116	122	144	1
14	Ponnaiyan	48	M	58	118	118	120	140	1
15	Annamalai	32	F	54	116	114	126	154	1
16	Madhavan	42	M	58	116	112	124	148	1
17	Mahalingam	39	F	52	116	120	128	148	1
18	Ramesh	24	M	53	120	120	124	156	1
19	Rajeshwari	25	F	50	118	124	130	154	1
20	Vijayan	31	M	54	124	122	132	150	1
21	Vanajakshmi	34	F	48	120	124	136	146	1
1	Meenatchi	42	F	50	76	68	86	122	1
2	Shanthi	22	F	54	78	72	98	124	1
3	Sundari	33	F	56	84	70	96	132	1
4	Shankar	24	M	53	86	72	92	126	1
5	Rajeshwari	25	F	50	88	74	88	128	1
6	Vijayan	31	M	54	82	72	84	122	1
7	Vanajakshmi	34	F	48	80	72	88	116	1
8	Devendran	27	M	48	78	70	92	118	
9	Rani	35	F	54	74	68	84	108	
10	Nirmala	28	M	48	72	66	88	112	
11	Mani	36	F	56	76	70	92	116	
12	Eswaran	21	M	50	84	80	96	122	

GROUP II–HEART RATE CHANGES (beats per minute)

13	Lakshmi	48	F	58	82	74	94	116	
14	Govindammal	48	F	60	84	74	98	128	
15	Rangarajan	49	M	58	68	64	118	116	
16	Selvam	37	M	56	68	62	114	118	
17	Chitra	38	F	50	68	66	118	114	
18	Arockiyamary	37	F	50	74	68	114	112	
19	Balu	21	M	54	70	66	112	110	
20	Maragatham	25	F	50	74	70	110	112	

GROUP II – SYSTOLIC BLOOD PRESSURE CHANGES (mm Hg)

7	Varalakshmi	34	F	50	130	128	132	152	14
8	Devendran	27	M	48	134	132	136	158	14
9	Rani	35	F	54	134	134	138	159	15
10	Nirmala	28	M	48	130	130	134	156	14
11	Mathavan	36	M	56	124	124	132	144	14
12	Eswaran	52	M	60	126	124	136	150	13
13	Lakshmi	48	F	58	128	124	136	152	14
14	Govindammal	68	F	66	130	126	134	150	14
15	Ranganayan	42	M	58	132	130	134	156	14
16	Selvam	37	M	56	134	132	138	146	14
17	Chitra	38	F	56	136	134	134	150	14
18	Arockiyamary	37	F	56	132	126	134	150	14
19	Balu	24	M	58	134	132	138	156	14
20	Latha	45	F	57	138	136	140	154	14
207	Murugatham	28	FM	54	178	304	180	950	16
8	Bhuvana	46	F	50	74	74	82	98	9
9	Gokul	33	M	56	72	76	80	102	9

GROUP III–HEART RATE CHANGES (beats per minute)

10	Nalini	22	F	48	76	70	80	98	9
11	Ramalingam	48	M	53	84	72	82	94	9
12	Renuka	24	F	45	82	80	82	98	9
13	Pushpa	49	F	50	68	76	84	96	9
14	Sivaraman	36	M	50	84	68	80	69	8
15	Revathy	41	F	55	84	80	86	102	9
16	Monica	25	F	48	64	66	74	92	9
17	Angamuthu	44	M	57	74	72	78	98	9
18	Katherine	22	F	50	70	72	80	96	9
19	Krishnan	42	M	57	74	70	78	94	9
20	Balan	36	M	54	66	64	76	88	9

GROUP III – SYSTOLIC BLOOD PRESSURE CHANGES (mm Hg)

7	Kumar	28	M	54	116	116	114	128	1
8	Bhuvana	46	F	50	114	114	116	126	1
9	Gokul	33	M	56	120	118	122	132	1
10	Nalini	22	F	48	126	126	128	136	1
11	Ramalingam	48	M	58	122	120	124	130	1
12	Renuka	24	F	45	124	124	126	132	1
13	Pushpa	49	F	50	118	116	120	128	1
14	Sivaraman	36	M	52	110	108	112	128	1
15	Revathy	41	F	54	112	108	110	136	1
16	Ponnappan	39	M	56	122	118	116	142	1
17	Rani	42	F	52	120	122	124	139	1
18	Padmanaban	33	M	58	130	124	120	158	1
19	Pradeep	25	M	50	128	122	124	150	1
20	Balan	36	M	54	116	120	128	148	1

SYSTOLIC BLOOD PRESSURE (mm Hg)

Sl. No	Name	Age (yrs)	Sex	Weight (kgs)	Baseline	Pre Intubation	During Intubation	1 min after intubation	3 min after intubation
8	Punithavathy	28	F	50	74	68	90	100	1
9	Kathiravan	35	M	58	78	71	88	104	1

GROUP IV–HEART RATE CHANGES (beats per minute)

10	Muniyappan	21	M	55	82	69	82	110	9
11	Dinesh	35	M	60	86	62	68	132	1
12	Gowri	24	F	50	84	70	74	114	1
13	Senthil	42	M	58	80	72	78	105	9
14	Sudha	38	F	50	88	74	84	118	9
15	Sultan	26	M	50	82	66	76	122	8
16	Mercy	41	F	48	84	62	78	124	9
17	Muthu	44	M	54	68	64	82	104	8
18	Boopathy	32	M	53	74	68	80	114	7
19	Esther	48	F	56	76	72	84	108	7
20	Vijayanand	34	M	57	78	66	88	128	1

GROUP IV – SYSTOLIC BLOOD PRESSURE CHANGES (mm Hg)

	Punithavathy	28	F	50	116	108	106	132	
	Kathiravan	35	M	58	118	112	114	138	
	Muniyappan	21	M	55	114	110	116	136	
	Dinesh	35	M	60	108	104	112	122	
	Gowri	24	F	50	112	112	118	122	
	Senthil	42	M	58	124	122	124	152	
	Sudha	38	F	50	126	120	124	144	
	Sultan	26	M	50	128	122	128	148	
	Mercy	41	F	48	130	126	132	155	
	Muthu	44	M	54	132	128	130	152	
	Boopathy	32	M	53	128	122	128	146	
	Esther	48	F	56	110	104	112	134	
	Vijayanand	34	M	57	112	110	110	136	

OPTIMAL TIME FOR INJECTION OF SMALL DOSE FENTANYL FOR BLUNTING THE CIRCULATORY RESPONSES TO TRACHEAL INTUBATION

PROFORMA

NAME: AGE/SEX:
WEIGHT:
IP NO: RANDOM NO:
DIAGNOSIS:
SURGERY:

PRE OP EVALUATION:

BP: CVS: Breath Holding Time:
PULSE: RS:
Hb%:
ASA Classification: MPC Class:

STUDY GROUP:

GROUP I : Inj Pentazocine 500µg / kg 5 mins before intubation
GROUP II: Inj Fentanyl 2µg / kg 1 minute before intubation
GROUP III: Inj Fentanyl 2µg / kg 5 minutes before intubation
GROUP IV: Inj Fentanyl 2µg / kg 10 minutes before intubation

INCLUSION CRITERIA:

1) ASA I & II patients
2) MPC I&II patients
3) Age 10 to 60 years

EXCLUSION CRITERIA:

1) ASA III & IV patients
2) MPC CLASS III & IV patients
3) Age < 10 & >60 years
4) Obese Patients
5) Patients on cardiac drugs
6) Patients with HTN, DM, IHD, CRF
7) Intubation time > 15 secs

PREMEDICATION:

Tab Diazepam 10 mg PO; HS night before surgery
Tab Ranitidine 150 mg PO; 6 am on day of surgery

INDUCTION:

DRUG	DOSE	GIVEN
Inj Thiopentone Sodium	5 mg / kg	
Inj Vecuronium Bromide	0.1 mg / kg	
Inj Fentanyl citrate	2 µg / kg	
Inj Pentazocine	500 µg / kg	

PARAMETERS:

VARIABLE	SAP (mm Hg)	DAP (mm Hg)	MAP (mm Hg)	HR (per min)
Baseline				
Preintubation				
During Intubation				
1 Min After Intubation				
3 Mins After Intubation				

SIDE EFFECTS:

Hypertension	MAP >130% of baseline value or >130 mmHg whichever is higher	YES / NO
Hypotension	MAP < 70% of baseline value or < 65mm Hg	YES / NO
Tachycardia	HR > 120 bpm	YES / NO
Bradycardia	HR < 60 bpm	YES / NO
Dysrhythmia	Any ventricular or supraventricular premature beat or rhythm other than sinus	YES / NO
Skeletal muscle	Chest tightness, tight bag and mask	YES / NO

rigidity	ventilation	
Depression of spont. ventilation	Fall in SPO2 to < 92% in room air before thiopentone injection	YES / NO
Delayed recovery	failure of the patient to wakeup even 20 to 30 mins after the termination of anaesthesia	YES / NO
Postoperative resp. depression	fall in respiratory rate to < 12 and a fall in SPO2 value to < 92% in PACU	YES / NO

BIBLIOGRAPHY

1) Acalovschi I et al (1989) – The effect of fentanyl as an adjuvant to etomidate and thiopentone on the hemodynamic response to the induction of anaesthesia and intubation. Rev.Chir.Oncol.Radiology 1989 Sep-Oct; 38(5):387-96.

2) Adachi YU & Satamoto.M et al (2002) – Fentanyl attenuates the hemodynamic response to endotracheal intubation more than the response to laryngoscopy. Anaesth Analg.2002 Jul; 95(1):233-7.

3) Adachi.Y, Takamatsu.I & Harada.M et al (1998) – The effects of low doses of fentanyl, buprenorphine and Pentazocine on circulatory responses to endotracheal intubation. Masui 1998 Dec; 47(12):1478-81.

4) Batra.Y.K, Indu.B and Puri.GD (1988) – Attenuation of pulse rate and blood pressure response to laryngoscopy and tracheal intubation by clonidine. Int J Clin Pharmacol Ther Toxicol.1988 Jul; 26(7):360-3.

5) Black TE and Kay B et al (1984) – Reducing the hemodynamic responses to laryngoscopy and intubation. A comparision of alfentanil with fentanyl. Anaesthesia 1984 Sep; 39(9):883-7.

6) Chung.F and Evans.D (1985) – Low dose Fentanyl: hemodynamic response during induction and intubation in geriatric patients. Can Anaesth. Society J.1985; 32:622-8.

7) Chung.KS and Sinatra RS et al (1992) – The effect of an intermediate dose of labetolol on heart rate and blood pressure responses to laryngoscopy and intubation. J Clin Anaesth.1992 Jan-Feb; 4(1):11-5.

8) Curren.J and Crowley.M (1980) – Droperidol and endotracheal intubation. Anaesthesia 1980; 35:290.

9) Dahlgren.N and Messeter.K (1981) – Treatment of stress response to laryngoscopy and intubation with fentanyl. Anaesthesia 1981; 36:1022-6.

10) Denlinger.J.K and Ellison.N.E (1974) – Effect of intravenous lignocaine on circulatory responses to tracheal intubation. Anaesthesiology review 1974:3:13-15.

11) Donal.E.Martin et al (1982) – Low dose Fentanyl blunts circulatory responses to tracheal intubation. Anaesthesia Analgesia 1982; 61:680-4.

12) Donald.R.Miller and Raymond.J.Martinean (1989) – Bolus administration of esmolol for treatment of intraoperative myocardial ischemia. Canadian Journal of Anaesthesiology 1989- 36:5:593-597.

13) Durrani.M and Barwise JA et al (2000) – Intravenous chloroprocaine attenuates hemodynamic changes associated with direct laryngoscopy and tracheal intubation. Anaesth Analg. 2000 May; 90(5):1208-12.

14) Ebert JP and Pearson JD et al (1989) – Circulatory responses to laryngoscopy: the comparative effects of placebo, fentanyl and esmolol.Anaesth.1989 Nov; 39(6):112-8.

15) Fassoulaki.A and Kaniaris.P (1983) – Intranasal administration of nitroglycerine attenuates the pressor response to laryngoscopy and intubation of the trachea. British Journal of Anaesthesia.1983 Jan; 55(1):49-52.

16) Forbes A.M and Dally F.G (1970) – Acute hypertension during induction of anaesthesia and endotracheal intubation in normotensive man. British Journal of Anaesthesia 1970:42:618.

17) Fusciardi J and Godget.G et al (1986) – Role of fentanyl and nitroglycerin in prevention of myocardial ischemia associated with laryngoscopy and tracheal intubation in patients undergoing operations of short duration. Anaesth Analg.1986 June; 65(6):617-24.

18) Gaubatz CL & Wehner R.J (1991) – Evaluation of esmolol and fentanyl in controlling increases in heart rate and blood pressure during endotracheal intubation.A Anasth J 1991 Feb;59(1):91-6.

19) Glignone M and Quintin L (1986) – Effects of clonidine on narcotic requirements and hemodynamic responses during induction of fentanyl anaesthesia and endotracheal intubation. Anaesthesiology 1986; 64:36-42.

20) Goyagi T and Tanaka M et al (2005) – Landiolol attenuates the cardiovascular responses to tracheal intubation. J anaesth.2005; 19(4):282-6.

21) Hatano.Y et al (1989) – Intravenous administration of isosorbide dinitrate attenuates the pressor response to laryngoscopy and intubation. Acta Anaesthesiol Scand.1989 Apr; 33(3):214-8.

22) Kautto UM (1982) – Attenuation of the circulatory response to laryngoscopy and intubation by fentanyl. Acta Anaesthesiol Scand.1982 June; 26(3):217-21.

23) Kautto UM (1983) – Effect of combination of topical anaesthesia, fentanyl, halothane or N2O on circulatory response in normo and hypertensive patients. Acta Anaesthesiol Scandinavia 1983; 27:245-57.

24) King.B.D.Harris, L.C.Jr.Creifenstein, F.E.Elder J.D.Jr and Dripps R.D (1951) – Circulatory responses to direct laryngoscopy and tracheal intubation performed during general anaesthesia - Anaesthesiology 1951:12:556

25) Kitamura T and Yamada Y et al (2001) – Attenuation of hemodynamic responses to tracheal intubation by the Styletscope. British J Anaesth.2001 Feb; 86(2):275-7.

26) Licker.M and Farinelli.C et al (1995) – Cardiovascular reflexes during anaesthesia induction and tracheal intubation in elderlypatients: the influence of thoracic epidural anaesthesia. J Clin Anaesth.1995 Jun; 7(4):281-7.

27) Lindgren.L and Saarnivaara.L et al (1987) – Protection of fentanyl against cardiac dysrhythmias during induction of anaesthesia. Eur. J Anaesth.1987 Jul; 4(4):229-33.

28) McCammon.R.L, Hilgenberg.J.C and Stoelting.R.K (1981) – Effect of Propranolol on circulatory responses to induction of diazepam-nitrous oxide anaesthesia and to endotracheal intubation. Anaesthesia Analgesia.1981 Aug; 60(8):579-83.

29) Mikawa.K and Goto.R et al (1991) – Effects of Pindolol on cardiovascular response to tracheal intubation. British Journal of Anaesthesia.1991 Oct; 67(4):416-20.

30) Mikawa.K and Kaetsu.H et al (1991) – Effects of Adenosine Triphosphate on the cardiovascular response to tracheal intubation. British J Anaesth.1991 Oct; 67(4):410-5.

31) Mikawa.K and Maekawa.N et al (1991) – Effects of Diazoxide on the cardiovascular response to tracheal intubation. J Int Med Res.1991 Jan-Feb; 19(1):32-8.

32) Mikawa.K and Yaku.H et al (1992) – Effects of mexilitine on the hemodynamic responses to tracheal intubation. J Int Med Res.1992 Apr; 20(2):121-6.

33) Mikawa.K et al (1992) – Effects of Nilvadipine on the cardiovascular responses to tracheal intubation. J Clin Anaesth.1992 Jul-Aug; 4(4):292-6.

34) Miller.C.D and S.J.Warren (1990) – Intravenous lignocaine fails to attenuate the cardiovascular response to laryngoscopy and tracheal intubation. British Journal of Anaesthesia: 65:216-219.

35) Milocco I and Axson et al (1985) – Haemodynamic stability during anaesthesia induction and sternotomy in patients with IHD: a comparision of six different techniques. Acta Anaesthesiology Scandinavia 1985; 29:465-73.

36) Nishikawa.T and Namiki.A (1989) – Attenuation of pressor response to laryngoscopy and tracheal intubation with intravenous Verapamil. Acta Anaesthesiol Scand.1989 Apr; 33(3):232-5.

37) Nishina.K & Mikawa.K et al (1995) – Fentanyl attenuates cardiovascular responses to tracheal extubation. Acta Anaesthesiol Scand 1995 Jan; 39(1):85-9.

38) Nishino.T.Hiraga.K and Sugimori.K (1990) – Effects of lignocaine on airway reflexes elicited by irritation of tracheal mucosa in human anaesthetized with enflurane. British Journal of Anaesthesia 1990: 64:682-687.

39) Pang.W.W & Lei CH et al (1999) – The effects of Tramadol versus fentanyl in attenuating hemodynamic response following tracheal intubation. Acta Anaesthesiology Sin.1999 Dec; 37(4):191-6.

40) Prys Roberts.C, Green.L.T, Meloche.R and Foe.P (1971) – Haemodynamic consequences to laryngoscopy and endotracheal intubation. British Journal of Anaesthesia 1971:43:531.

41) Reilly.C.S, Wood A.J.J., Wood.M (1985) – Variability of Fentanyl pharmacokinetics in man. Computer predicted plasma concentration for three intravenous dosage regimens – Anaesthesia 1985:40:837-843.

42) Ryhanen.P, Saarela.E, Saukkonen.J and Hollmen.A (1977) – Circulatory responses to laryngoscopy and intubation in patients with or without cardiovascular disease. Effect of prophylactic Practolol. Ann Chir Gynaecol.1977:66(6):294-98.

43) Sahihoglu.Z & Demiroluk.S (2002) – Comparision of effects of remifentanil, alfentanil and fentanyl on cardiovascular responses to tracheal intubation in morbidly obese patients. Eur JAnaesthesiol.2002 Feb; 19(2):125-8.

44) Saitoh.N and Mikawa.K et al (1992) – Effects of Trimethophan on the cardiovascular response to tracheal intubation. British Journal Of anaesthesia 1992 Feb; 68(2):228.

45) Sims CH and Splinter WM (1990) – Fentanyl blunts the hemodynamic response of children to laryngoscopy. Can J Anaesth.1990 May; 37(4 Pt 2):S91.

46) Smith J.E & King.M.J et al (1992) – Effect of fentanyl on the circulatory responses to orotracheal fibreoptic intubation. Anaesthesia 1992 Jan; 47(1):20-3.

47) Splinter WM and Cervenko F (1989) – Hemodynamic responses to laryngoscopy and tracheal intubation in geriatric patients: effects of fentanyl, lidocaine and thiopentone. Can J Anaesth.1989 Jul;36(4):370-6

48) Steimhans J.E and Lewis Gaskin (1963) – A study of intravenous lidocaine as a suppressant of cough reflex – Anaesthesia: 24:285.

49) Stoelting RK (1979) – Attenuation of blood pressure response to laryngoscopy and tracheal intubation with Sodium Nitroprusside. Anaesth Analgesia 1979; 58:116-9.

50) Stoelting.R.K (1978) – Blood pressure and heart rate changes during short duration laryngoscopy for tracheal intubation- influence of viscous or intravenous lidocaine. Anaesth Analgesia 1978; 57:197-9.

51) Tam.S, Chung.F and Cambell.J.M (1985) – Attenuation of circulatory responses to endotracheal intubation using intravenous lignocaine; a determination of the optimal time of injection. Canadian Journal of Anaesthesia-32: S 65.

52) Tammisto.T and Aromaa.U (1977) – The role of different components of balanced anaesthesia in tolerance to endotracheal intubation. Ann Chirg Gynaecol Suppl.1977; 66(5):254-57.

53) Wycoff.C.C (1960) – Endotracheal intubation – Effects on blood pressure and pulse rate. Anaesthesiology: 21:153.

54) Yoo KY and Jeong ST et al (2003) – Nitrous oxide attenuates pressor but augments norepinephrine response to laryngoscopy and endotracheal intubation. Anaesth Analg.2003 May; 96(5):1516-21.

55) Young Jin and Kim et al (1998) – Small dose Fentanyl: Optimal time of injection for obtunding the circulatory response to tracheal intubation. Anaesthesia Analgesia 1998; 86:658-61.